VOLUME 42 NUMBER 3 SEPTEMBER, 1956

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

CONTENTS

Tumors of the anterior visual pathways ..... *Frank B. Walsh* 347
Retinopathy of immaturity ..... *Hedwige Habegger ..... F. Randolf Philbrook, Francis J. Curley and Theodore H. Ingalls* 377
Hawaii through the ophthalmoscope ..... *William John Holmes* 393
Sclerocleisis ..... *A. B. Vicencio* 402
Aqueous-humor lactate concentration ..... *Bernard Becker and Marguerite A. Constant* 406
Biomicroscopy of posterior eye ..... *Hans Rotter* 409
Hysteria and malingering ..... *Harvey A. Lincoff and Jerome Ennis* 415
Removal of sclerocorneal sutures ..... *Brian J. Curtin and Truman L. Boyes* 421
Ethylene-oxide sterilization .. *R. A. Skeehan, Jr., J. H. King, Jr., and Saul Kaye* 424
Phosphorus metabolism in the lens ..... *H. K. Müller, O. Kleifeld, H. P. Arens, U. Dardenne, R. Fuchs and O. Hockwin* 431
Critical flicker frequency ..... *Irwin Feinberg* 473
Metimyd: A clinical study ..... *Ira A. Abrahamson, Jr., and Ira A. Abrahamson, Sr.* 482
Lighting for tangent screen ..... *Myles M. Berk* 486
Carrier for cataract-mask string ..... *Peter Chao* 487
Pocket flashlight .... *Conrad Berens, George Z. Carter and Arnold S. Breakey* 488
Metaherpetic keratitis ..... *Algernon B. Reese* 489

DEPARTMENTS

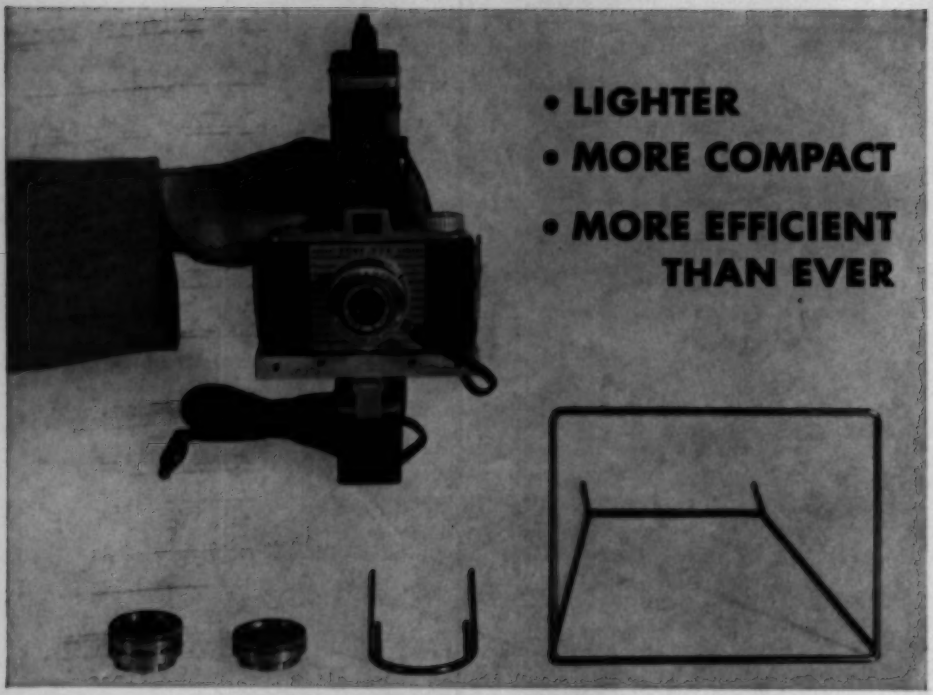
Society Proceedings 490 Obituary ..... 506 Book Reviews 508
Editorial ..... 504 Correspondence ... 507 Abstracts 510
News Items 530

For complete table of contents see advertising page xxv

Publication office: 450 Ahnaip St., Menasha, Wisconsin

Copyright, 1956, Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois

Subscription price in United States twelve dollars yearly. In Canada and foreign countries fourteen dollars. Published monthly by the Ophthalmic Publishing Company. Subscription and Advertising Office: 664 North Michigan Avenue, Chicago 11, Illinois. Entered as second class matter at the post office at Menasha, Wisconsin. Printed in U.S.A.



New Clini Camera D

only **$150.00**

See a demonstration of this beautifully-designed instrument that incorporates Camera and Strobe-type flash in one unit.

On display at the 1956 meeting of the American Academy of Ophthalmology and Otolaryngology.

Jenkel-Davidson
OPTICAL COMPANY

American Academy of Ophthalmology
Booths 103-105, Exhibition Hall, Palmer House, Chicago
366 POST STREET • SAN FRANCISCO, CALIFORNIA

"a small hurt in the eye is a great one"
—H. G. Bohn

Terra-Cortril assures the eye maximum protection from infectious organisms and accompanying inflammation. The corticosteroid-antibiotic combination appears to be synergistic.[1]

supplied:
In amber bottles, with sterile eye dropper, containing 5 mg. oxytetracycline hydrochloride (TERRAMYCIN®) and 15 mg. hydrocortisone (CORTRIL®) per cc.

also available: CORTRIL Acetate Ophthalmic Ointment and CORTRIL Tablets.

1. Robinson, H. M., Jr., et al.: M. Times 83:227, 1955.

Terra-Cortril®
brand of oxytetracycline and hydrocortisone
ophthalmic suspension

Pfizer
PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

The Traveling Man from Mager & Gougelman

Eddie Kerr has helped physicians fit thousands of patients with artificial eyes. Like the other experts from our offices, he provides you with technical information and assistance on difficult cases. The samples in his case will match many patients. Or, he can make eyes that perfectly match with the materials he carries. One of our experienced men visits most areas regularly—another reason to call or write our nearest office for your next ocular prosthesis.

Complete Glass and Plastic Artificial Eye Service

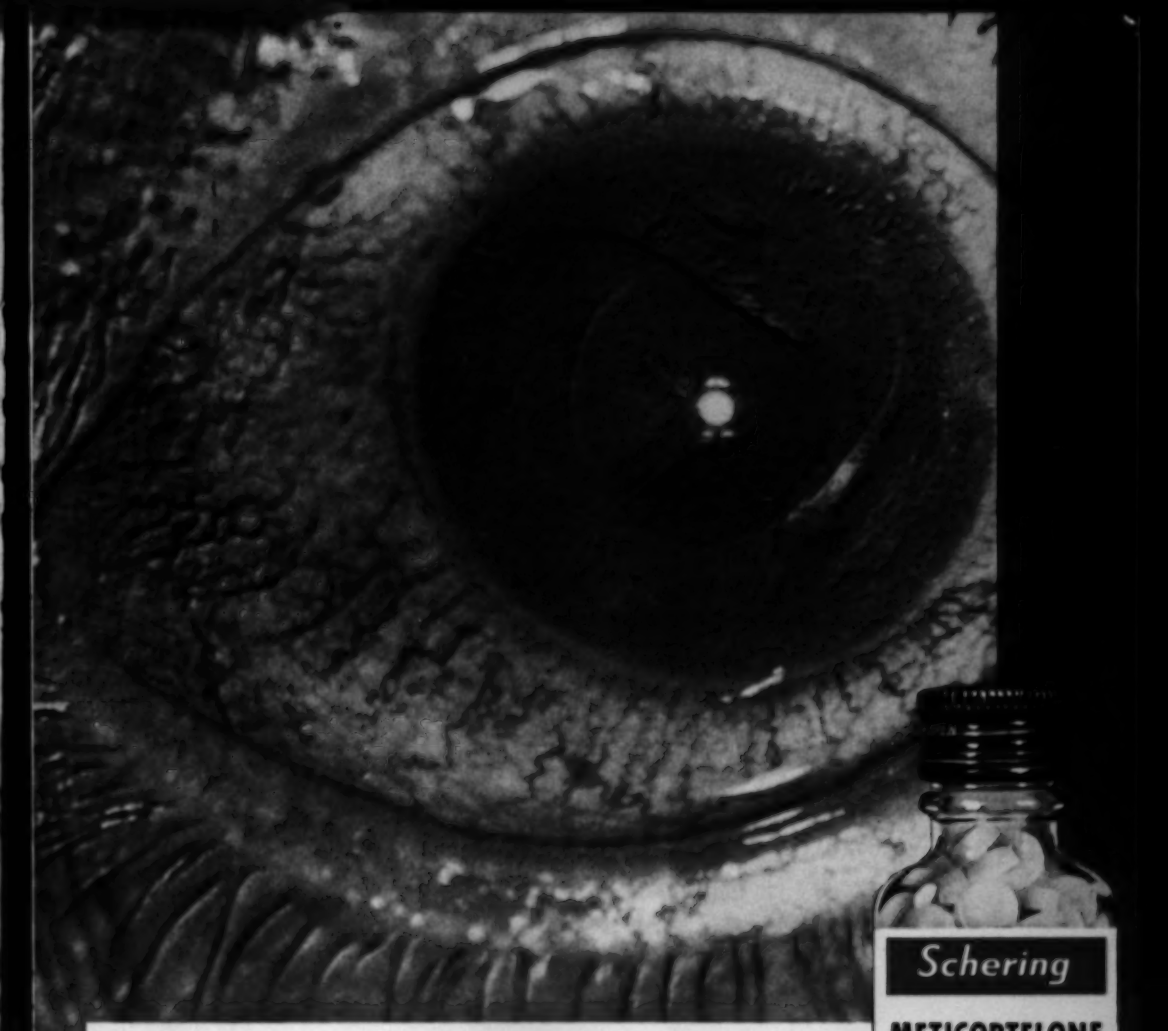
- Made to order and selections from stock
- Eyes sent on memorandum same day order received
- Damaged or broken artificial eyes accurately matched
- Fitted to all types of motility implants
- Implants, X-Ray therapy shields, foreign body locators
- Superior Quality—Finest Workmanship

Serving the Profession Since 1851

Mager and Gougelman inc.

30 North Michigan Avenue, Chicago 2, Illinois : 510 Madison Avenue, New York 22, New York

DETROIT • CLEVELAND • KANSAS CITY • MINNEAPOLIS • ST. LOUIS
BOSTON • PHILADELPHIA • PITTSBURGH • WASHINGTON



patients with allergic and inflammatory

eye disorders

and their physicians deserve the benefits of

METICORTELONE®

(PREDNISOLONE)

for patient

prompt relief of ocular distress...no weight gain to guard against...no difficult dietary rules

for physician

far smaller dosage than with oral hydrocortisone...no undue worry about edema, sodium retention, potassium loss...patient cooperation assured...simplifies control of a wide variety of inflammatory and allergic disorders

buff-colored tablets of 1, 2.5 and 5 mg.

ML-J-2075

METICORTELONE,® brand of prednisolone.

No "before-and-after" demonstration amazes like that of the old flint Kryptok and incomparable Orthogon "D"! You don't need a "practiced" eye to see instantly the clear, sharp, color-free imagery of Orthogon "D"—and its far greater reading range. Orthogon "D" Nokrome combination of crown glass and barium glass segment focuses rays of all colors at a given point. Which would YOU wear?

They Look Alike... But What a Difference!

IN ENGINEERING

IN PERFORMANCE

ORTHOGON "D"

"the invisible bifocal"

BAUSCH & LOMB

Upjohn

Delta-Cortef* for inflammation, neomycin for infection:

Neo-Delta-Cortef†

TOPICAL OINTMENT

Each gram contains:

Delta-1-hydrocortisone acetate 5 mg. (0.5%)

Neomycin sulfate.....5 mg.
(equiv. to 3.5 mg. neomycin base)

Methylparaben.....0.2 mg.

Butyl-p-hydroxybenzoate 1.8 mg.

Supplied: 5-gram tubes

EYE-EAR OINTMENT

Each gram contains:

Delta-1-hydrocortisone acetate 2.5 mg. (0.25%)

Neomycin sulfate.....5 mg.
(equiv. to 3.5 mg. neomycin base)

Supplied: ⅛ oz. tubes with applicator tip

*TRADEMARK

†TRADEMARK FOR THE UPJOHN BRAND OF PREDNISOLONE ACETATE WITH NEOMYCIN SULFATE

The Upjohn Company, Kalamazoo, Michigan

storz Surgical Instruments

Improved

Hot Air Sterilizer •

To Prevent Corrosion of Sharp **Eye Instruments**

E-7070

Sterilizer, Hot Air: features dry heat, constant temperature forced circulation for even distribution of heat, well insulated for economy and room comfort, fully automatic.

Hot air sterilization eliminates the corrosive damage to sharp, delicate eye instruments so frequent in boiling, autoclaving and some cold sterilizing agents. High temperature is well below point at which temper of sharp instruments would be affected.

Hot air sterilization eliminates bothersome refilling and cleaning of water sterilizer and portable autoclave.

Price: $247.50

Special Features

- Does not draw in outside air.
- Circulation of air in sterilizer chamber insures constant temperature in all areas.
- Good insulation reduces current consumption.
- Even preheating and cooling prevents overheating in any area.
- Fully automatic; requires no attendance after starting, and no special wiring or connections.

Outside dimensions are 20" long, 12" wide, and 15" high. Each of the three trays measures 11" long, 5" wide and 1¼" deep.

Total useful capacity 11" x 6¾" x 7¼".

Weight 40 lbs.

Fully Automatic Controls include INTERNAL TIMER, VISUAL THERMOMETER and INDICATOR LIGHT.

Simplified Operation

After instruments are placed in the sterilizer, the switch at the right rear is moved forward. This includes the time switch in the circuit. The time clock is then set for the required sterilization and preheating time. The preheating time is 20 minutes and normally sterilization time is 30 minutes, a total of 50 minutes. The temperature control knob is set at between 180° and 200° centigrade as desired. Then turn on control switch for operation, which is above the red light on the front. The red light indicates that the sterilizer is on. Thermometer on top of sterilizer can be checked to determine if inside temperature is correct.

For uninterrupted operation of the sterilizer the time clock switch at the right rear should be pushed back. This removes the time clock from the circuit.

Alternate current (AC) only, 110 Volt, 50-60 Cycle.

Order directly from:

Storz Instrument Company

4570 Audubon Ave.
St. Louis 10, Mo.

Too convenient to forget: steroid-antibiotic drops

(HYDROCORTISONE ACETATE-NEOMYCIN SULFATE, MERCK)

'HYDROPTIC' provides double benefits. It guards vision by reducing inflammation and combating infection. Neatly packaged in unbreakable plastic, 'HYDROPTIC' vials fit any purse or pocket, provide precise dropper action and protect the contents from contamination.

Supplied: In 5-cc., plastic squeeze vials containing either 0.5% (5 mg./cc.) or 2.5% (25 mg./cc.) 'HYDROCORTONE' Acetate plus 5 mg. of neomycin sulfate per cc.

MSD

MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC. PHILADELPHIA 1, PA.

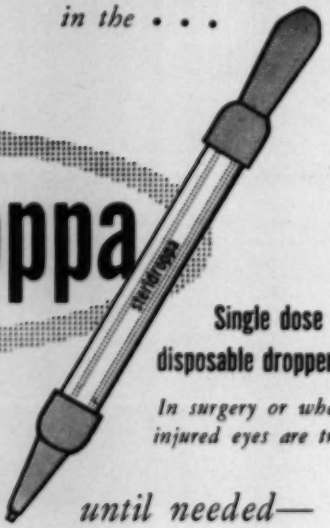
COMPLETE CONFIDENCE *with* OPHTHALMOS

sterile, fully potent eye medications

in the . . .

steridroppa

U.S. Pat. Off. 2,707,469



Single dose
disposable dropper unit

In surgery or wherever injured eyes are treated

Sealed until needed—

Sterile at the moment of use.

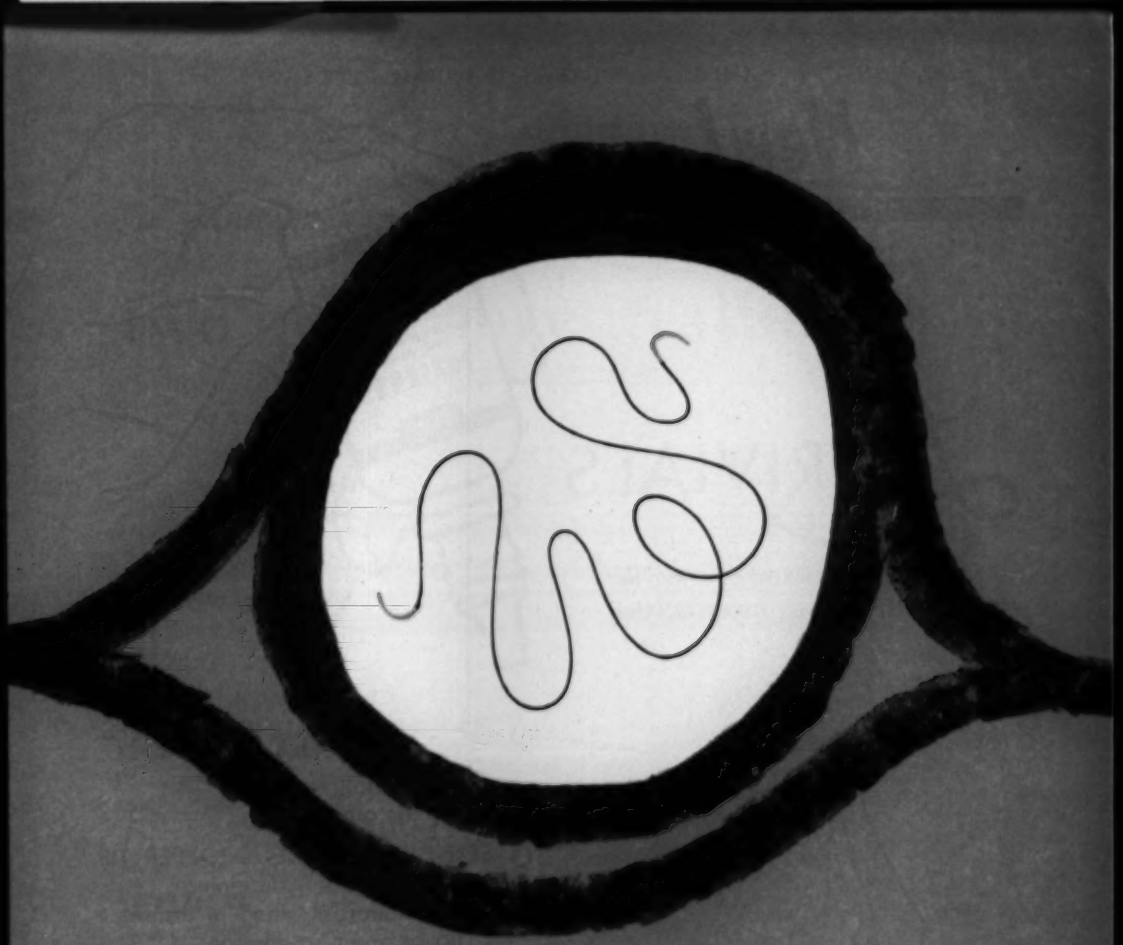
A snip of the scissors cuts the sealed tip, and the **steridroppa** is ready to use.

A sterile single dose of ophthalmic drug in a properly buffered and preserved solution. Like injectable solutions, packed in autoclaved glass and rubber, and sealed until the moment it is needed. Mishandling and contamination eliminated.

Substantial size and weight of the **steridroppa** provides ease in handling and full control of instillation. Vari-colored insoluble ceramic imprints provide permanent rapid identification at all times.

ALL IMPORTANT SOLUTIONS REQUIRED IN THE OPERATING ROOM ARE AVAILABLE IN THE STERIDROPPA IN HANDY PACKAGES OF 6 OR HOSPITAL SIZE PACKAGES.

Write now for details to **OPHTHALMOS, Inc.**
Union City, New Jersey



new needle sutures

for scleral resection and dacryocystorhinostomy

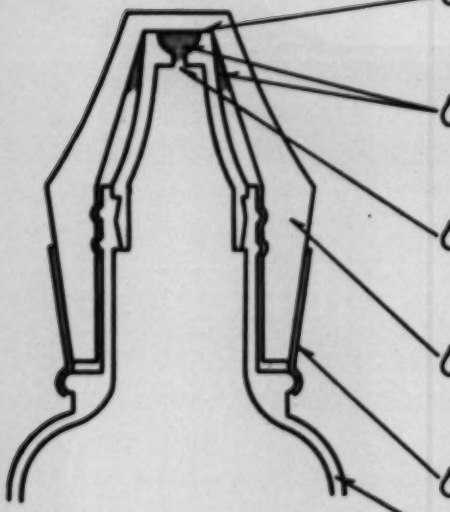
double-armed ophthalmic needle-sutures with special MICRO-POINT® needles designed in consultation with leading ophthalmologists for use in particularly delicate procedures.

ETHICON®

New!

LACRIVIALS

ISO-SOL's brand of sterile polyethylene dropper bottles



- **FLAT INNER SEALING SURFACES**
  Leakproof
  No crystallization
  Avoids gumming
- **SELF-DISINFECTING DROPPER TIP**
  Bacteriostatic containing medication, retained to disinfect tip between instillations
- **CONTROLLABLE DROPPING ORIFICE**
  Cannot spill
  Cannot leak
  Sucks back unused medication
- **TRANSPARENT CAP**
  Visible seal
  Unbreakable
  Color coded
- **TAMPER-PROOF OUTER SEAL**
- **LIGHTWEIGHT UNBREAKABLE BOTTLE**

Available:

Atropisol Bonazin Bonmiotin Butacaine Carbamiotin Esromiotin
Fluorescein M-Z Solution Phenylzin Pilomiotin Tearisol Tetracaine

Send for free sample box of Lacrivials

THE ISO-SOL CO., INC., ISO-SOL BROOKLYN 17, N. Y.

for glaucoma therapy

two new concentrations of

ISOPTO® CARPINE

.25% and 3%

sterile ophthalmic solutions

NOW . . . a full range of concentrations for the treatment and control of glaucoma . . . and other conditions where miosis is desired!

ISOPTO® Carpine
Pilocarpine HCl in .5%
Methyl Cellulose Solution
.25%
.5%
1%
2%
3%
4%

ISOPTO® Eserine
Eserine Salicylate in .5%
Methyl Cellulose Solution
.25%
.5%

advantages . . .

- *Sterile, Stable*
- *Prolonged Contact*
- *Greater Comfort*
- *Always Uniform*
- *Greater miscibility with tears*
- *pH and tonicity adjusted*
- *Preserved against contamination*

ISOPTO® Designates Alcon's Sterile Ophthalmic Solutions containing Methyl Cellulose.

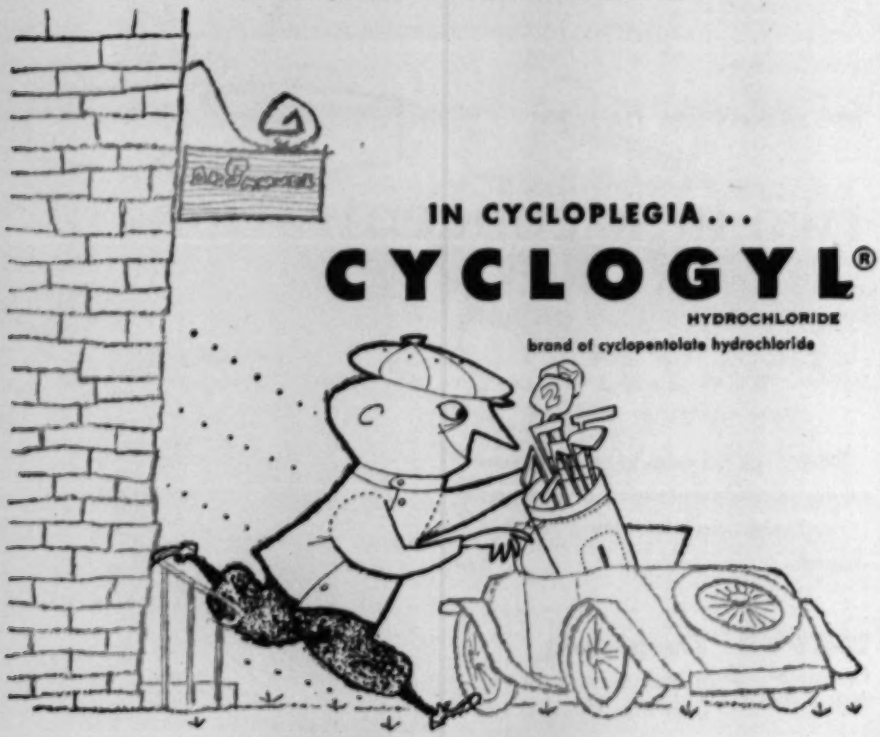
Available from pharmacies and wholesale drug suppliers throughout the U.S.A. and Canada (Canadian distributors, Imperial Optical Co., Toronto)

Packaged and sealed in Alcon's exclusive non-spillable, non-breakable DROP-TAINER® (15 cc). Reduces contamination possibilities . . . convenient to use.

Alcon

laboratories, inc. fort worth, texas

AL-IC-1



IN CYCLOPLEGIA . . .

CYCLOGYL®

HYDROCHLORIDE

brand of cyclopentolate hydrochloride

SAVES TIME

. . . for you . . . with rapid onset of action

. . . for your patients . . . with rapid recovery

"Cyclopentolate hydrochloride . . . produces a rapid [30 to 60 minutes], intense cycloplegia and mydriasis of moderate duration . . . and is effective in highly pigmented irises and for persons of all ages." *New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Company, 1954, p. 189.*

Cyclogyl has shown outstanding qualities in 1035 cases.[1]
(Incorporates work of 11 previous investigators)

Compound	Dosage and Administration (drops) *	Diopters of Residual Accommodation	Spontaneous Recovery (in hours)
Cyclogyl 0.5%	2	1.10	24†
Homatropine 2% or 4%	2	2.00	48

*Successive drops at five-minute intervals.

†Recovery time reduced to six hours after one-percent pilocarpine.

1. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. 38:831 (Dec.) 1954.

"the chief handicap of maximum cycloplegia, namely its incapacitating effect, is minimized . . ." *Gunn, B. C.: A.M.A. Arch. Ophth. 51:467 (Apr.) 1954.*

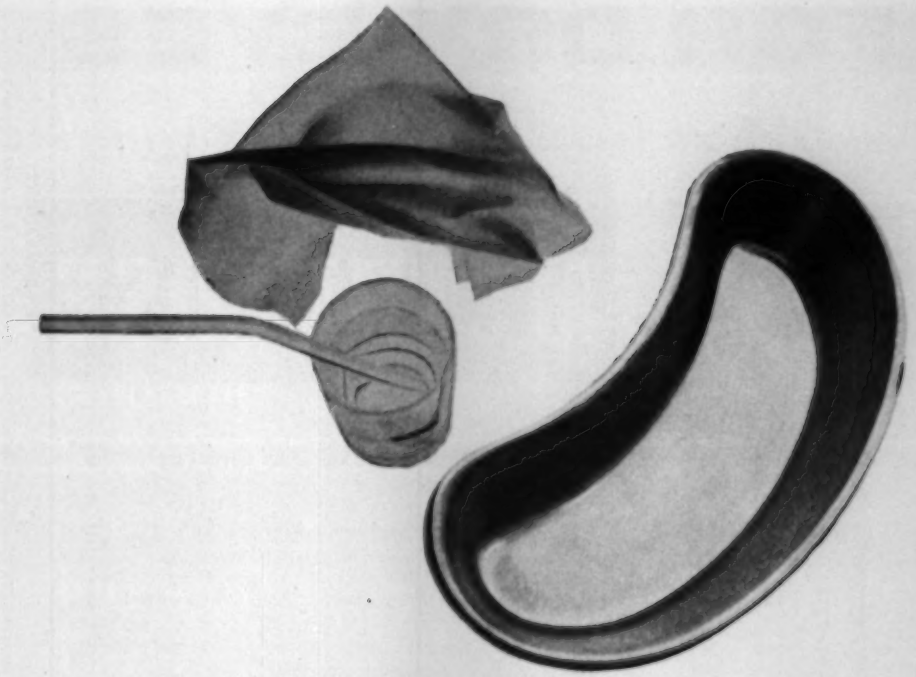
Cyclogyl, "by virtue of its brevity, rapidity of action, and consistent depth of cycloplegia, will be [a drug of choice] for routine refraction . . ." *Ehrlich, L. H.: New York J. Med. 53:3015 (Dec. 15) 1953.*

Dosage:
Cycloplegia – One drop 1.0%, in each eye (or two drops of 0.5%) produces maximal cycloplegia in 30-60 minutes. Recovery time is normally 4-12 hours spontaneously. Pilocarpine reduces recovery time. In deeply pigmented eyes, 2 drops of 1.0% in each eye, instilled 10 minutes apart, achieves satisfactory cycloplegia in 98% of cases.
Mydriasis – One or two drops of 0.5% in each eye.

Samples and Literature on request.

Supplied:
Sterile ophthalmic solution in Gifford's Buffer (pH 6.0)
0.5% Solution – 15 cc Dropper Bottles
1.0% Solution – 15 cc Dropper Bottles
2 cc Dropper Bottles

Schieffelin & Co Since 1794
Pharmaceutical and Research Laboratories
New York 3, N. Y.
In Canada: William Sofin Ltd., Montreal 25, P.Q.



THORAZINE*

"markedly inhibits postoperative vomiting."[1]

With 'Thorazine' "postoperative retching seldom is a problem. Intractable nausea and retching due to spinal anesthetics responded . . . Retching caused by organ manipulation also responded."[1]

'Thorazine' administered before general anesthesia "reduced the postoperative vomiting from 28.8 per cent to 13 per cent."[2]

1. Mathews et al.: Am. Pract. & Dig. Treat. 6:360 (Mar.) 1955.
2. Albert and Coakley: Anesth. & Analg. 33:285 (July-Aug.) 1955.

'Thorazine' is available in ampuls, tablets and syrup, as the hydrochloride; and in suppositories, as the base.

'Thorazine' should be administered discriminately; and, before prescribing, the physician should be fully conversant with the available literature.

Smith, Kline & French Laboratories, 1530 Spring Garden Street, Philadelphia 1

**T. M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.*

FOR DRY EYES

OR

AS A VEHICLE - - - CONTACT LENS FLUID

BUFOPTIC

METHULOSE

METHULOSE is an ideal substitute for lacrimal secretions in Kerato-Conjunctivitis Sicca. It spreads smoothly throughout the conjunctival sac, relieving the feeling of "dryness" and reducing irritation.

METHULOSE will not clog eye lashes or blur vision. It is stable, does not support bacterial or fungal growth, and is unaffected by light or long standing. Complete comfort is assured the patient.

As a Vehicle

METHULOSE is compatible with many drugs commonly used in Ophthalmology. Atropine Sulfate, Pilocarpine HCl and Homatropine HBr. may be added in therapeutic amounts.

Contact Lens Fluid

The lubricating and emollient action of **METHULOSE** enables the patient to wear contact lenses comfortably for long periods of time.

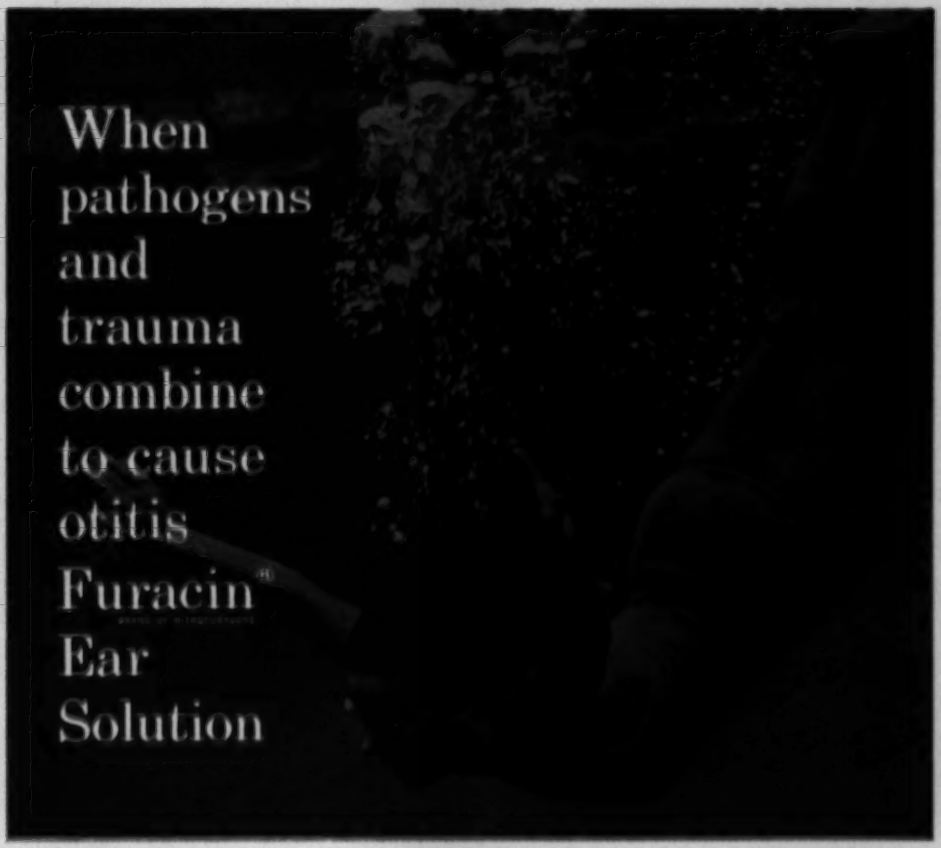
METHULOSE is a non-irritating, buffered Methylcellulose solution. Preserved with Benzalkonium chloride U.S.P. 1:25,000. Supplied in the new 15cc. Plastic container, and hermetically sealed 15cc. and 30cc. screw cap glass vial, dropper enclosed.

Write for samples and literature on complete line of ophthalmic solutions.

Professional Pharmacal Co., Inc.
Pharmaceutical Manufacturers
San Antonio, Texas

METHULOSE, a brand of Methylcellulose, is the registered trademark of PROFESSIONAL PHARMACAL CO., INC.

"Manufacturers of fine ophthalmic solutions since 1943"



When pathogens and trauma (such as ear picking, swimming and diving) combine to cause otitis, FURACIN Ear Solution can be expected to provide prompt antibacterial[1] and deodorizing action.[2]

ADVANTAGES OF FURACIN IN THE TREATMENT OF EXTERNAL OTITIS:

- exceptional antibacterial range
- nonirritating
- nondrying—high concentrations of the drug combat organisms for long periods
- nonstaining; odorless
- anhydrous

"There was a total of 65 chronic discharging ears, of which 44 became dry with the initial or second course of FURACIN therapy for an incidence of 67.7 per cent . . . The significance of these results, however, lies in the fact that 49 out of 55 patients (89 per cent) had been previously treated by one or more otologists with failure to obtain a permanently dry ear."[3]

DIRECTIONS: Cleanse meatus well with irrigation and drying. Instill 1/3 dropperful (0.5 cc.) 3 or 4 times daily. Patient should remain with treated ear upward for several minutes. Insert cotton plug. Impregnated wick may be used.

FORMULA: FURACIN 0.2% in hygroscopic, water-soluble, polyethylene glycol. Dropper bottle of 15 cc.

REFERENCES: 1. Anderson, J. R., and Steele, C. H.: Laryngoscope 58:1279, 1948. 2. Long, P. H.: A-B-C's of Sulfonamide and Antibiotic Therapy, Philadelphia, W. B. Saunders Co., 1948, p. 152. 3. Peele, J. C.: Laryngoscope 63:488, 1953.

For infections of the eye and nose:

FURACIN OPHTHALMIC

- liquid
- ointment

Rapid, effective antibacterial action with unique lack of irritation.

FURACIN NASAL

- with ephedrine
- with Neo-Synephrine*

Topically effective antibacterial with vasoconstrictor.

NITROFURANS

a new class of antimicrobials neither antibiotics nor sulfonamides

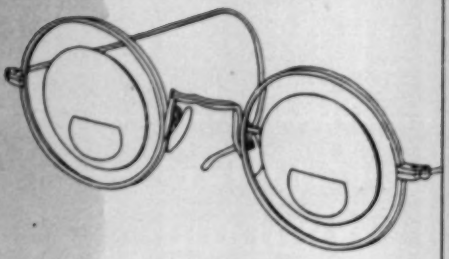
Eaton Laboratories
Norwich, New York

*Neo-Synephrine—reg. trademark Winthrop Laboratories, Inc., brand of phenylephrine.

CASE HISTORY #3

Case History #3 explains the usefulness of Catarex Service in cases of bilateral cataract extractions. In this case, immediate vision was especially important, since the patient, a diabetic, lived alone and had to administer insulin to herself daily.

This case history emphasizes the fact that CATAREX T temporary cataract bifocals have proved themselves more versatile in aphakic cases *than any other form of temporary lens.* CATAREX T lenses are a simple answer to the old, complicated problem of easing the patient through the post-operative period. Why not use this splendid service on *your* next cataract case? Your optician or laboratory will be happy to supply details.



CASE HISTORY – Mrs. Y. Y.

A 67-year-old diabetic female had a left extracapsular lens extraction on October 26, 1954, and one week later, November 2, 1954, had a right intracapsular lens extraction. The post-operative course was normal. Patient was discharged November 10.

11-18-54: The patient was given the right and left +10.00 CATAREX T (temporary) lenses which had been ordered for her soon after discharge from the hospital. That she could avail herself of such a service was important, for she lived alone and had to administer insulin to herself daily.

11-23-54: Manifest O.D. +12.00Dsph. = 20/70—. Manifest O.S. +12.00Dsph. = 20/70+. Rx: these in CATAREX T (temporary style) straight-top bifocals. Until these were received by the patient, she continued to wear the previous lenses. This policy was followed in all subsequent changes, so the patient was never without a pair of CATAREX T bifocals.

12-16-54: Manifest O.D. +12.00 = 20/20—; Manifest O.S. +13.00 = 20/30. Rx: these in CATAREX T bifocals.

1-6-55: Manifest O.D. +12.00Dsph. ○ +1.00Dcyl. ax 165 = 20/15+; Manifest O.S. +11.00Dsph. ○ +1.00Dcyl. ax 90 = 20/20—. Rx: these in CATAREX T bifocals.

1-14-55: Manifest O.D. +13.50Dsph. ○ +1.00Dcyl. ax 165 = 20/15; Manifest O.S. +12.50Dsph. ○ +1.00Dcyl. ax 90 = 20/20+. Rx: these in CATAREX T bifocals.

4-21-55: Manifest O.D. +13.00Dsph. ○ +1.00Dcyl. ax 180 = 20/15+; Manifest O.S. +13.00 Dsph. ○ +1.00 Dcyl. ax 150 = 20/20. Rx: these in CATAREX T bifocals.

7-18-55: Manifest O.D. +13.25Dsph. ○ +1.00Dcyl. ax 180= 20/15+; Manifest O.S. +13.00Dsph. ○ +0.75Dcyl. ax 135 = 20/20+; +2.75D add = Jg. 0.75 @ 13". Rx: these in permanent CATAREX D bifocals.

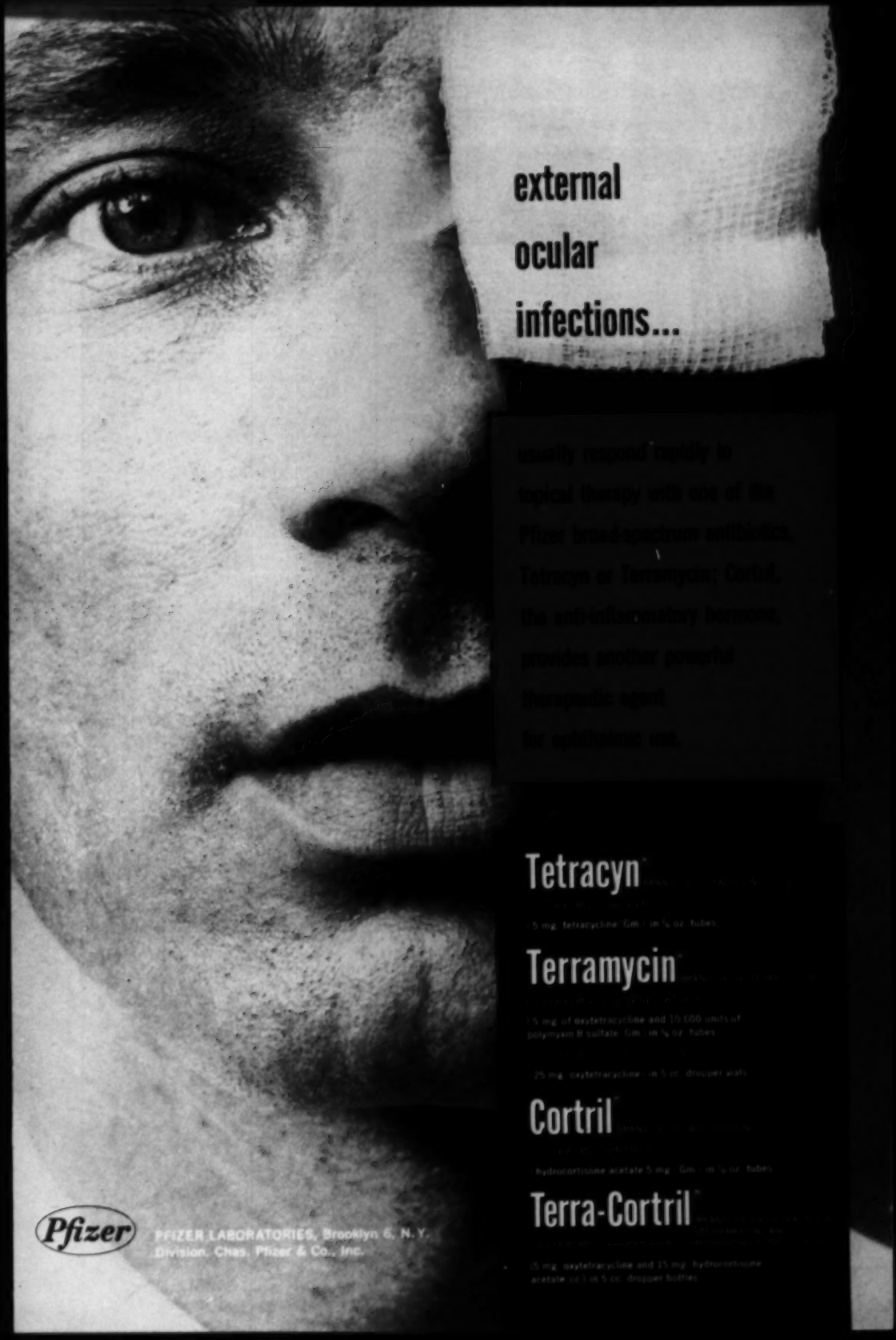
3-7-56: With permanent CATAREX D of 7-18-55, the right vision = 20/15+; the left vision = 20/20+.

The patient received her first pair of CATAREX T (temporary style) lenses eight days after discharge from hospital. She had six different pairs of temporary lenses during a period of eight months before the permanent CATAREX D bifocals were prescribed. Because she had useful vision throughout this period, there was no urgency to prescribe the permanent lenses. The importance of this is indicated by the fact that there was no need to change these lenses eight months after they were prescribed. The patient was not only made visually comfortable post-operatively and enabled to administer insulin to herself daily, but was spared the expenditure of the relatively large amounts which she could ill-afford, for several changes of the regular post-cataract bifocals, which would have been mandatory if the Catarex Temporary Service were not available to her.

CATAREX 'T'

TEMPORARY CATARACT BIFOCAL LENSES BY VISION-EASE

Manufacturers of a complete line of quality multifocals


external
ocular
infections...
easily respond rapidly to
topical therapy with one of the
Pfizer broad-spectrum antibiotics,
Tetracyn or Terramycin; Cortril,
the anti-inflammatory hormone,
provides another powerful
therapeutic agent
for ophthalmic use.
Tetracyn
5 mg. tetracycline Ointment in ⅛ oz. tubes
Terramycin
5 mg. of oxytetracycline and 10,000 units of polymyxin B sulfate Ointment in ⅛ oz. tubes
25 mg. oxytetracycline in 5 cc. dropper vials
Cortril
hydrocortisone acetate 5 mg. Ointment in ⅛ oz. tubes
Terra-Cortril
5 mg. oxytetracycline and 15 mg. hydrocortisone acetate per cc. in 5 cc. dropper bottles
Pfizer
PFIZER LABORATORIES, Brooklyn 6, N. Y.
Division, Chas. Pfizer & Co., Inc.

council accepted

new corneal anesthetic

rapid action and

short duration*

virtually **nonsensitizing**
no cases reported of dermatitis occurring in patient's eye or on hands of physician.

relatively **nonirritating**
does not sting or burn when dropped into the eye—changes in the corneal epithelium or hyperemia of the conjunctiva rarely occur.

Average dose: *for tonometry*, 2 drops. *For minor surgical procedures*, 2 drops instilled 3 times at 90 second intervals.

Supplied: sterile normal saline solution with 0.02% Butoben as preservative, and containing 0.4% Dorsacaine Hydrochloride (benoxinate hydrochloride). In ½ oz. plastic squeeze bottle with dropper tip which delivers uniform drops (approximately 45 drops per cc.).

*Schlegel, H. E., Jr., and Swan, K. C.: A. M. A. Arch. Ophth. 51:463 (May) 1954.

DORSACAINE®

HYDROCHLORIDE

SMITH-DORSEY • Lincoln, Nebraska • A Division of The Wander Company

Topically effective sight safeguards

STERILE OPHTHALMIC SUSPENSIONS
AND OPHTHALMIC OINTMENT

HYDROCORTONE®

ACETATE

(HYDROCORTISONE ACETATE, MERCK)

Topically administered hydrocortisone has proved to be "superior (to cortisone) in ...: contact dermatitis of the lids; vernal conjunctivitis; sclerosing keratitis; superficial punctate keratitis; recurrent corneal erosions, and diffuse episcleritis..." "Most other lid and anterior segment diseases responded equally well either to cortisone or hydrocortisone..."

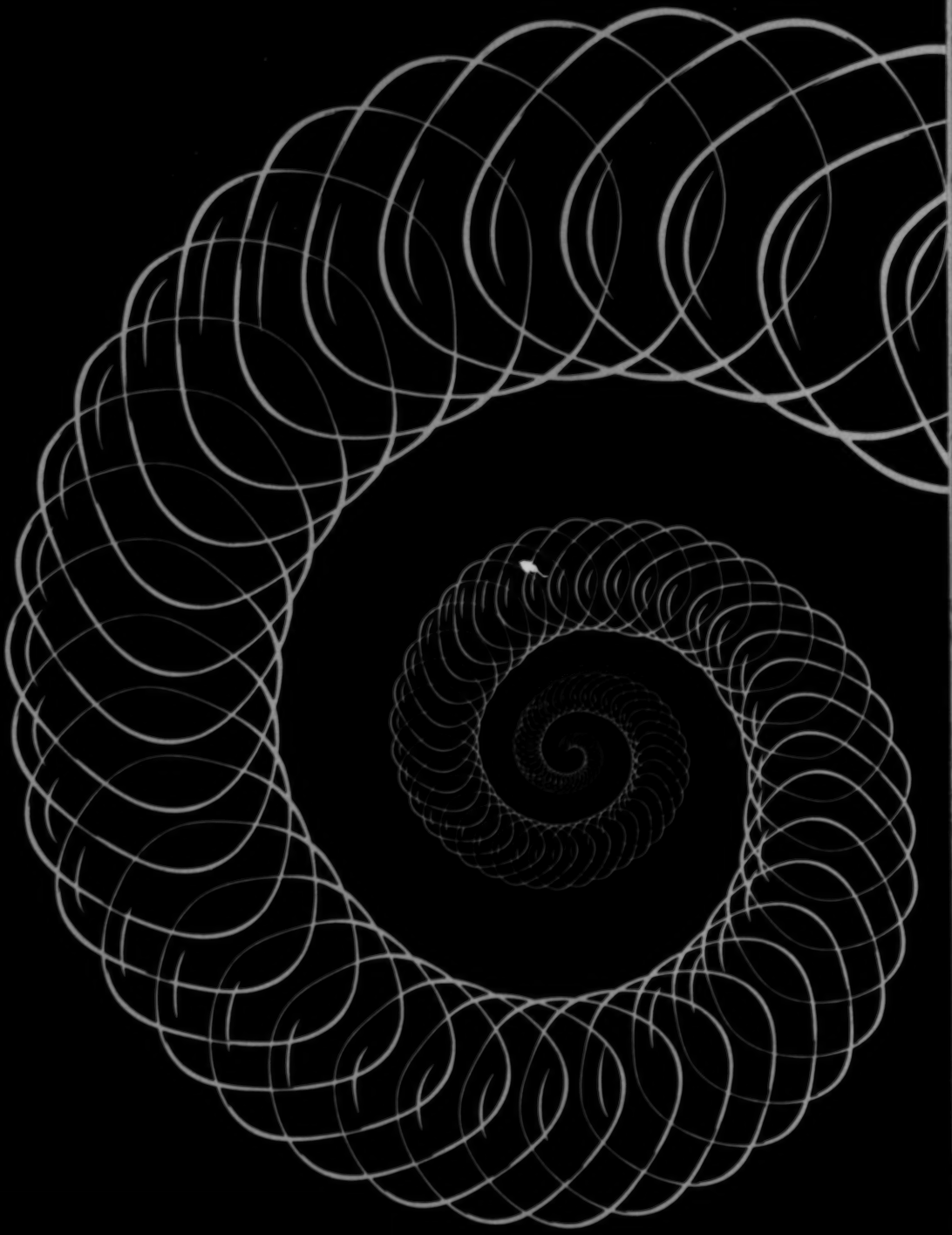
Supplied: Sterile Ophthalmic Suspensions of HYDROCORTONE Acetate—0.5 and 2.5 per cent; 5-cc. dropper bottles. Ophthalmic Ointment of HYDROCORTONE Acetate—1.5 per cent; 3.5-Gm. tubes.

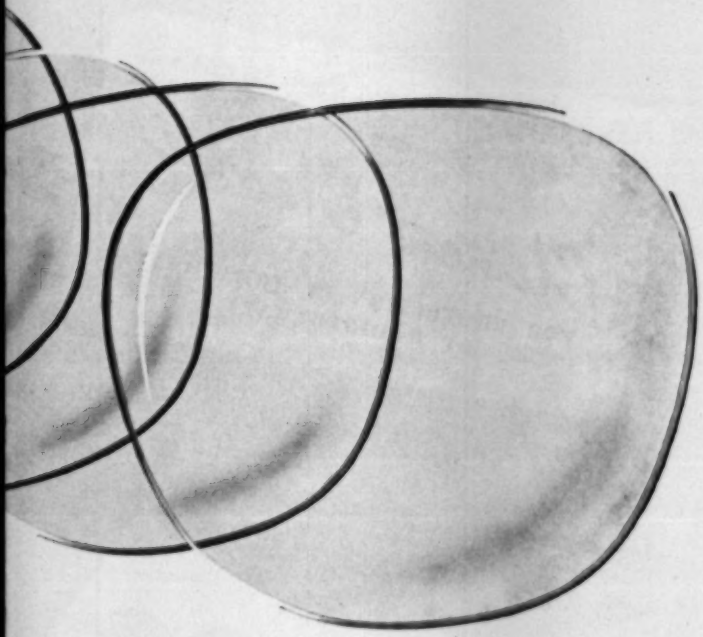
References: Hogan, M. J., Thygeson, P. and Kimuras, J., Arch. Ophth. 53:165, (Feb.) 1955.

MSD

MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.





Over...and over...and over again

Yes, by the hundreds, by the thousands, and now by the millions, the choice is WIDESITE®.

You know, of course, the advantages of the corrected curve. If, however, you are not familiar with WIDESITE'S qualities, please let us send you a copy of a recent technical brochure detailing in what ways we believe it is the finest corrected curve lens made.

WIDESITE'S performance, and its increasing preference, are important in making Shuron the world's largest organization devoted exclusively to serving the ophthalmic profession.

SHURON OPTICAL COMPANY, INC. SHURON® **Geneva, N.Y.**
Rochester, N.Y.

Pat. No. 530108

PERSPEX LINED LEAD SHELLS
BY
Clement Clarke
FOR PROTECTION IN TREATMENT
BY RADIOTHERAPY

Perspex lined lead shells in the form of a contact lens afford the eye complete protection when treating parts very close to the eye with X-rays or rays from radio-active substances. By drilling a small hole in the shell it is even possible to carry out localised treatment of a lesion on the sclerotic without exposing the cornea and other parts of the sclerotic to the harmful effects of the radiations. The set of lead shells illustrated comprises six sizes for both right and left eyes. Smaller cases and single shells are also available. *Price, complete in case—$97.30.*

CLEMENT CLARKE of England

63 WIGMORE STREET, LONDON, W.1, ENGLAND

New Univis lenses with **25mm.** segments

from stock for your Rx!

D-25 *Note the identifying tinted line*

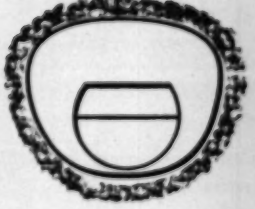
Univis Nu-Line D-25

The original Univis straight-top design—now in 25 mm. segment width when you need wider lateral field at near. *Also has special Nu-Line treatment developed for wide segment bifocals.* Prescribe for absolute security in the four vital areas of quality which *must* be built in by the manufacturer.

Univis CV6-25

You can now prescribe the original improved-type 3-foci multifocal with a 25 mm. segment—Univis. Highest standards of quality rigidly maintained. Rx for general purpose wear for 2.00 D reading add or greater.

Univis Nu-Line CV7-25



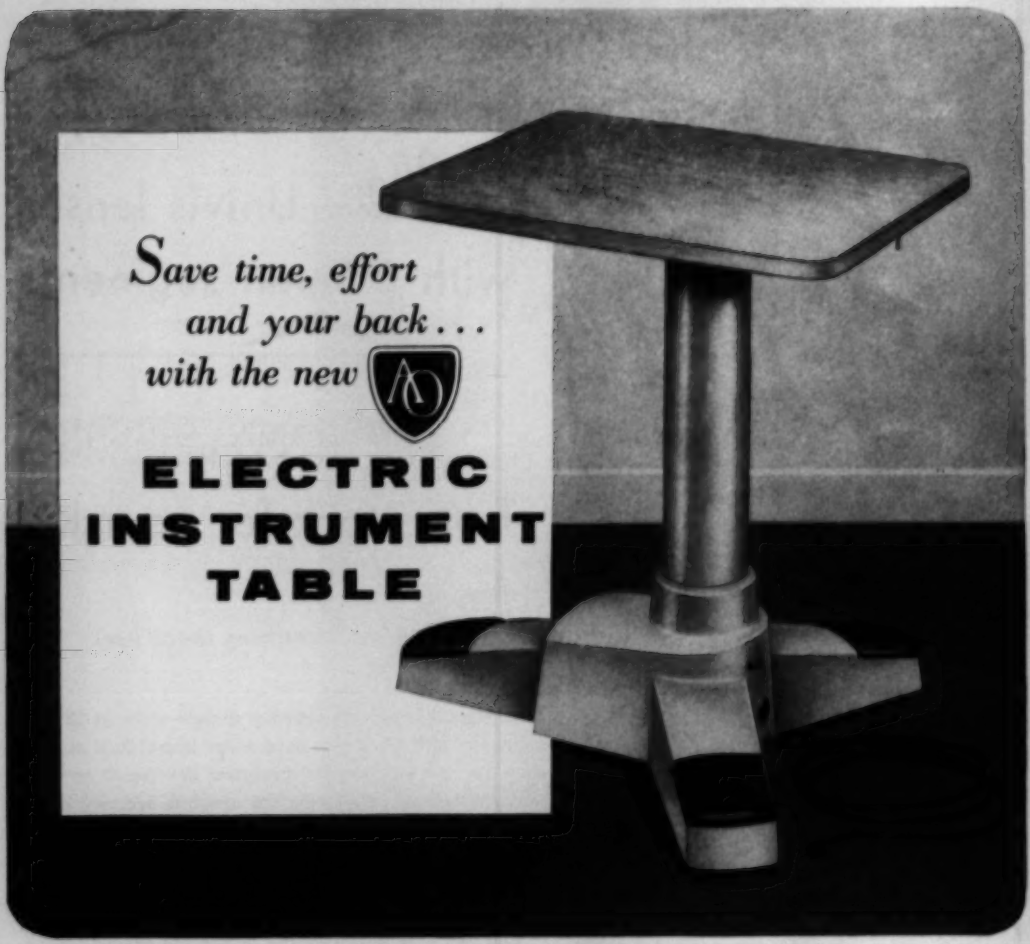
The popular Univis CV, specially treated to eliminate more than 80% of reflection and refraction by segment lines, now in 25 mm. segment width as well as in 23. Rx where reading add is greater than 2.00 D.

From stock, for wide lateral field at near and intermediate

UNIVIS

THE UNIVIS LENS COMPANY

Dayton, Ohio



Now! An end to under-the-table, backbreaking, awkward hand adjustments. At the flick of a finger the top of this new AO Electric Instrument Table glides up and down . . . total excursion, 11¼" . . . instantly reversible without overtravel. Instruments are effortlessly positioned in proper relationship to your patient's eye level.

Spacious 19" x 22½" top covered in gray limed oak Panelyte . . . new hardsurfaced plastic material resistant to abrasion, chipping and wear. Amazing new EPOXY finish has remarkable adhesive qualities, is the most durable enamel known. Choice of three smart colors: jade green, ivory tan and coral add new beauty to your professional office. Rugged heavy-duty motor assures years of smooth, quiet operation . . . lifts at least 75 pounds.

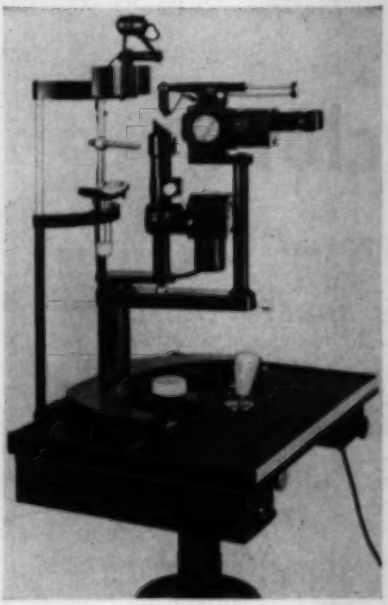
Since control switch is attached just under table top edge, switch is always at table top level, always readily accessible and always out of reach of patient. Convenient electric outlet for instrument use located in base. Complete table moves easily on swivel-type rubber casters.

Full information at nearly 300 AO Offices, or write

American Optical
INSTRUMENT DIVISION

† T.M. Reg. by American Optical Company

SLIT LAMP APPARATUS



ON INSTRUMENT TABLE OR COMPOUND STAGE, the latter designed for electric tables or refracting units.

Requires no adjustments. The slit lamp can be swung past the corneal microscope without interruption of observation.

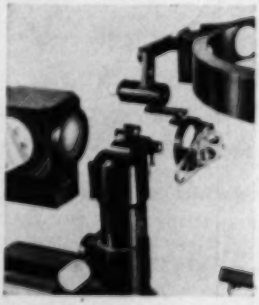
Can be set for five different magnifications by simply turning a knob, without changing objectives, eyepieces, or the working distance.

Maximum brilliance of the illuminating rays and sharpest possible definition of the microscope images.

Supplementary equipment, such as Hruby lens, gonioscope, photo attachment, etc., are available.

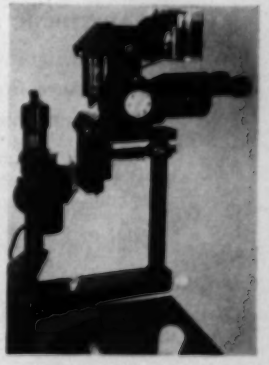
CARL ZEISS
IN WEST GERMANY

ACCESSORIES



ATTACHMENT FOR GONIOSCOPY (left) consisting of: 4-mirror contact glass with handle, carrier and rotating device. Rotatable prism in mount. To keep lid apart during examination we offer one each small and large lid separator.

PHOTO ATTACHMENT (right) with electronic flash equipment to automatically photograph anterior segment of eye at magnifications of 1x or 2x.

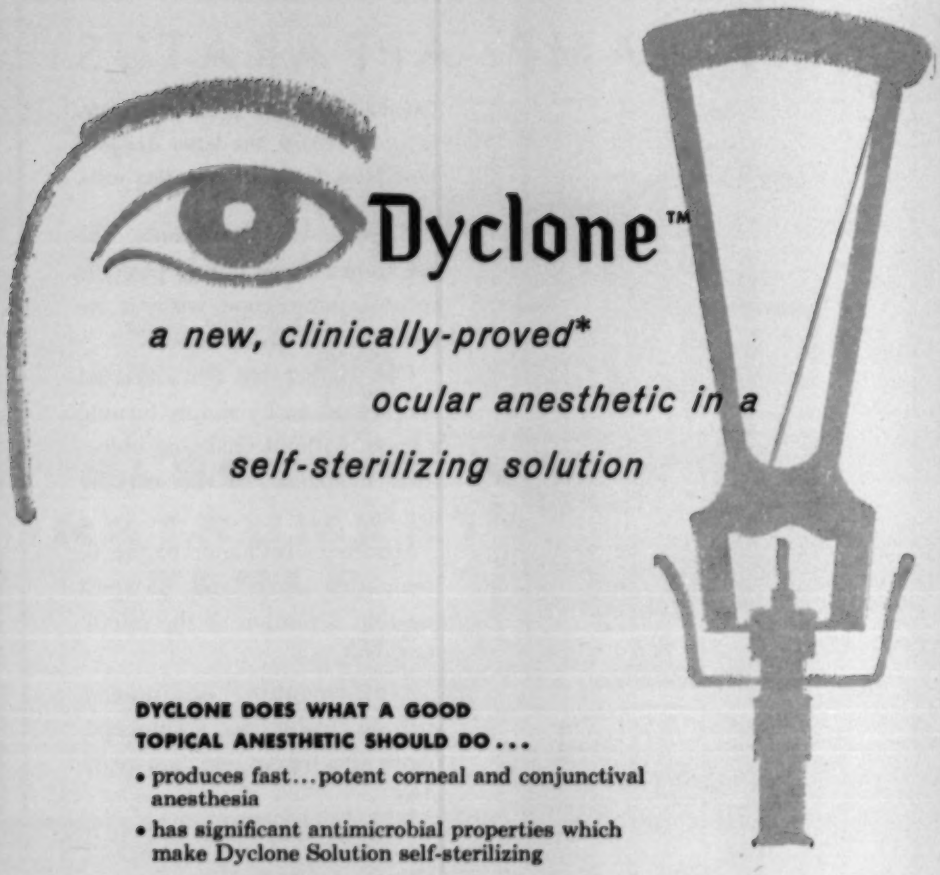


Write for literature

Visit our booths Nos. 72 and 73 at the forthcoming Meeting of the American Academy of Ophthalmology and Otolaryngology at the Palmer House in Chicago, October 14-19, 1956.

CARL ZEISS, INC., 485 Fifth Avenue, New York 17, N.Y.

Guaranteed Uninterrupted Repair Service



Dyclone™

a new, clinically-proved ocular anesthetic in a self-sterilizing solution*

DYCLONE DOES WHAT A GOOD TOPICAL ANESTHETIC SHOULD DO...

- produces fast...potent corneal and conjunctival anesthesia
- has significant antimicrobial properties which make Dyclone Solution self-sterilizing

WITHOUT DOING WHAT YOU'RE AFRAID AN ANESTHETIC MIGHT DO

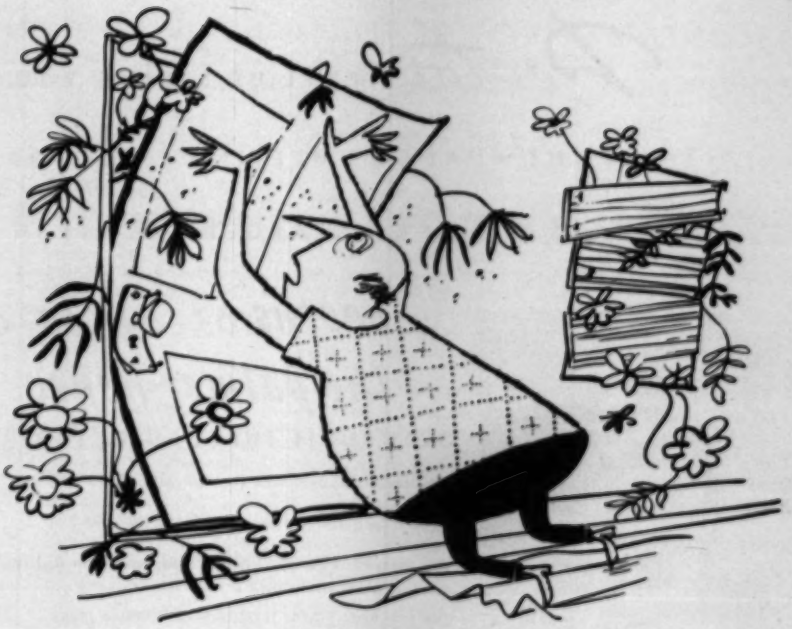
- has an insignificant incidence of sensitivity
- rarely causes irritation or inflammation
- won't cause miosis or mydriasis

Dyclone (dyclonine HCl), is an organic ketone, synthesized by Pitman-Moore Company. It is not a "caine" type compound.

Bottles of 1 oz.

*Arora, Consul, Sharma and Kulshrestha: E.E.N.T. Monthly 34: 593, 1955. Hungerford, L. N., Jr.: Bull. Mason Clin. 9:108, 1955. Swan, K.C.: Trans. Acad. Ophth. and Otolaryn. (in press)

PITMAN-MOORE COMPANY • *Division of Allied Laboratories, Inc.* • **Indianapolis 6, Indiana**



there's no escape from pollen . . .
help speed relief with Estivin
safely soothe irritated ocular
and nasal membranes with **sterile**

ESTIVIN®

a specially prepared infusion of *Rosa gallica L* (rose petals) preserved with 1:10,000 sodium ethylmercurithiosalicylate.

NONTOXIC . . . EFFECTIVE . . . EASY TO USE

Estivin Stops Itching, Burning, Excessive Lacrimation

• in hay fever • in allergic conjunctivitis and rhinitis • in the common cold

One drop of Estivin in the inner canthus of each eye three or four times daily is usually sufficient for day-long relief. In cases of extreme nasal discomfort, additional relief may be obtained by placing one or two drops in each nostril.

Estivin is supplied in 0.25 fl. oz. bottles with eye dropper.

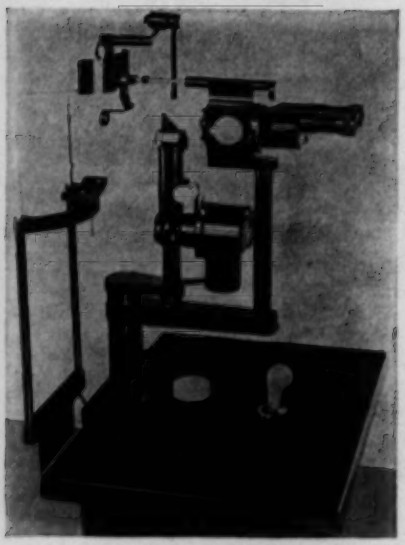
SAMPLES AND LITERATURE AVAILABLE ON REQUEST

Schieffelin & Co. Pharmaceutical and Research Laboratories since 1794
New York 3, N.Y.
In Canada: William Sofin Ltd., Montreal 25, P.Q.

Doctor: WE'LL BE SEEING YOU

AT THE ACADEMY MEETING IN OCTOBER

AT *our* NEW ENLARGED LOCATION



booths 63- 64- 65- 66

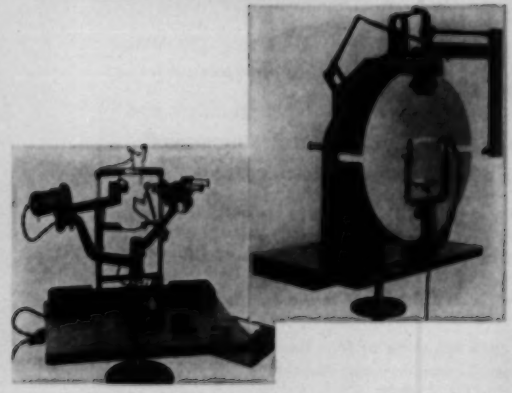
the palmer house

OCTOBER 14 THROUGH OCTOBER 19

you'll want to see

a complete line of foreign and domestic ophthalmic instruments including a new illuminated gonioscopy microscope, a new trial lens cabinet, a new ophthalmoscope *and* the Gunkel Screen

the complete line of fine Haag-Streit precision instruments—Goldmann Slit Lamp, Goldmann Perimeter, Goldmann-Weekers Adaptometer, Pflueger Perimeter, Aplanation Tonometer, and others



famous Zeiss equipment including Zeiss-Oberkochen Slit Lamp and Zeiss Refractionometer

examples of unusual lens grinding by H.O.V. technicians

latest frame styles including exclusive H.O.V. designs

The House of Vision Inc.

30 NORTH MICHIGAN, CHICAGO
MILWAUKEE • MINNEAPOLIS • DES MOINES
MASON CITY • SIOUX CITY
MUSKEGON • DAVENPORT

AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3 · VOLUME 42 · NUMBER 3 · SEPTEMBER, 1956

CONTENTS

ORIGINAL ARTICLES

The ocular signs of tumors involving the anterior visual pathways: The tenth Francis I. Proctor Lecture. Frank B. Walsh (with the assistance of John W. Chambers and Lois A. Lloyd) 347
Retinopathy of immaturity: In the newborn mouse after exposure to oxygen imbalances. Hedwige Habegger, F. Randolf Philbrook, Francis J. Curley, and Theodore H. Ingalls 377
Hawaii through the ophthalmoscope. William John Holmes 393
The scleral insert (sclerocleisis) for glaucoma: A preliminary report of three cases. A. B. Vicencio 402
The alterations in aqueous-humor lactate concentration: Following systemic carbonic anhydrase inhibition. Bernard Becker and Marguerite A. Constant 406
Technique of biomicroscopy of the posterior eye. Hans Rotter 409
Differential diagnosis of hysteria and malingering: In functional amblyopia: Report of a case. Harvey A. Lincoff and Jerome Ennis 415
The removal of sclerocorneal sutures. Brian J. Curtin and Truman L. Boyes 421
Ethylene-oxide sterilization in ophthalmology. R. A. Skeehan, Jr., J. H. King, Jr., and Saul Kaye 424
The phosphorus metabolism in the lens. H. K. Müller, O. Kleifeld, H. P. Arens, U. Dardenne, R. Fuchs and O. Hockwin 431
Critical flicker frequency in amblyopia ex anopsia. Irwin Feinberg 473
Metimyd: A clinical study. Ira A. Abrahamson, Jr., and Ira A. Abrahamson, Sr. 482

NOTES, CASES, INSTRUMENTS

A lighting system for a two-meter tangent screen. Myles M. Berk 486
Carrier for cataract-mask string. Peter Chao 487
A pocket flashlight with interchangeable tips: Designed especially for eye examinations. Conrad Berens, George Z. Carter and Arnold S. Breakey 488
Metaherpetic keratitis: Notes on treatment. Algernon B. Reese 489

SOCIETY PROCEEDINGS

Swiss Ophthalmological Society, September 30 to October 2, 1955 490
Yale University Clinical Conference, May 13, 1955 491
New England Ophthalmological Society, March 16, 1955 493
College of Physicians of Philadelphia, Section on Ophthalmology, March 17, 1955 496
New York Society for Clinical Ophthalmology, March 7, 1955 498

EDITORIAL

Intracranial bruits 504

OBITUARY

Henry Cooper Haden 506

CORRESPONDENCE

An aid to teaching gonioscopy 507

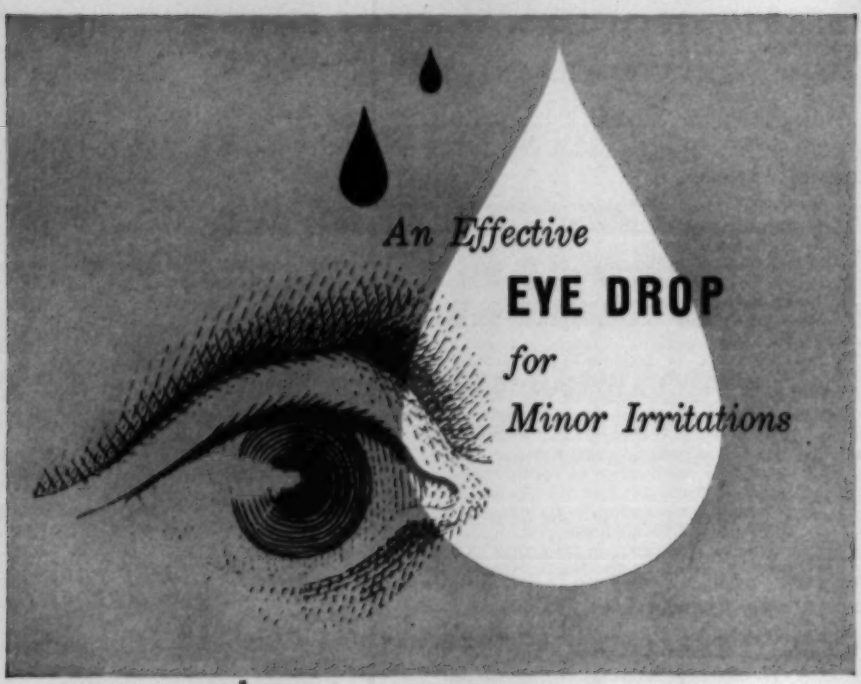
BOOK REVIEWS

Advances in Ophthalmology 508
The Story of Blindness 508
Geometrical Optics 509

ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension 510

NEWS ITEMS 530



OpH *contains*

Neo-Synephrine® HCl
—a prompt, long acting decongestant.

Boric acid
—nonirritating bacteriostatic and gentle antiseptic.

Zinc sulfate
—soothing astringent and mild antiseptic.

OpH® Eye Drops

DECONGESTANT • ASTRINGENT • ANTISEPTIC

for minor ocular irritations

Supplied in handy individual dropper bottles of 15 cc.—for easy instillation and maintenance of sterility.

OpH and Neo-Synephrine (brand of phenylephrine), trademarks reg. U.S. Pat. Off.

Winthrop LABORATORIES • NEW YORK 18, N. Y.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 42 SEPTEMBER, 1956 NUMBER 3

THE OCULAR SIGNS OF TUMORS INVOLVING THE ANTERIOR VISUAL PATHWAYS*

THE TENTH FRANCIS I. PROCTOR LECTURE

FRANK B. WALSH, M.D.

Baltimore, Maryland

(With the assistance of JOHN W. CHAMBERS, M.D., and LOIS A. LLOYD, M.D.)

My invitation to deliver the Proctor Lecture is an honor which I shall always prize highly. I decided that my best present effort might be in a review paper on the diagnosis of tumors affecting the optic nerves and chiasm. At the outset it seemed wise to limit the cases used to those in which tumor was verified by microscopic examination and, with this in mind, I visualized tables which would have statistical value.

As the work progressed my plans were altered. If only verified tumors were used, many interesting and instructive cases must be excluded—and accurate diagnosis often is not dependent upon laboratory work. In consequence, some unverified tumor cases have been utilized. It became obvious that, in several categories, I did not have sufficient cases that tables concerning them could have any statistical value. When to this last consideration was added an admitted incapacity for figures, there seemed to be valid reasons to make the paper nonstatistical.

Excepting in the sections dealing with intrinsic tumors of the optic nerves and chiasm, a deliberate effort has been made to exclude histologic-pathologic descriptions, since such material is available in standard texts as written by individuals who are experts in that field.

I am pleased to acknowledge much help from Dr. John Chambers, particularly as regards neurosurgical matters. Dr. Lois Lloyd has done a great deal of the work. I am grateful to her.

The paper is divided into two principal sections:

1. Intrinsic tumors involving the optic nerve and chiasm.

2. Extrinsic tumors affecting the optic nerve and chiasm. The types of tumors include meningiomas, craniopharyngiomas, pituitary tumors, malignant nasopharyngeal tumors, and third-ventricle tumors, as well as unusual tumor cases. Short sections are written on hypophysectomy for metastatic tumors and arachnoiditis.

I. INTRINSIC TUMORS INVOLVING THE OPTIC NERVE AND CHIASM

What is presented in this part of the paper is approximately what was presented before the Academy of Ophthalmology and Otolaryngology in October, 1955. An effort has been made to include all cases of intrinsic tumor that have come under my observation (table 1).

Sex. There were 17 females and nine males in this series.

Age. Incidence. Below one year, one; one to five years, six; five to 10 years, seven;

* From the Wilmer Ophthalmological Institute and the Department of Neurosurgery, The Johns Hopkins University and Hospital. Presented at the University of California Medical Center at San Francisco, December 9, 1955.

TABLE 1

OBSERVED CASES OF INTRINSIC TUMORS INVOLVING THE OPTIC NERVES AND CHIASM

Total number of cases	26	(22 verified)
Optic nerve tumors	10	(8 verified)
(gliomas 5; meningiomas 3; unproven 2, including a metastatic tumor of the disc)		
Optic chiasm tumors	16	(14 verified)
(gliomas 12; meningioma 1; undifferentiated carcinoma 1; 2 unverified tumors probably were gliomas. In one of these last-named cases neurofibromatosis was present)		

10 to 15 years, five; 15 to 53 years, seven (24, 27, 32, 40, 44, 53, 53 years).

Mortality. Eight of the 26 patients died but, since we were unable to obtain a follow-up in several instances, this figure means little or nothing. One death was in an adult woman several days after operation as a result of meningitis. Five patients died within days or a week or two after operation. In one instance, death was a result of cardiac arrest during encephalography.

TYPES OF TUMORS IN THIS SERIES OF CASES

The tumors were diagnosed as gliomas (astrocytomas, oligodendrogliomas), meningiomas (endotheliomas), and neurofibromas. Melanoma originating in the optic nerve was not observed; the series did contain one proven metastatic tumor but no example of an angioma. Brief mention is made of all these various tumors.

Melanomas. Melanoma originating in the optic nerve is observed infrequently. Melanoma of the choroid extending to involve the disc is seen more often, and we have records on five such cases. Melanomas involving the optic disc are seen most frequently in Negroes and such tumors are in most instances benign. It is of extreme interest that malignant melanoma of the choroid is an extremely rare tumor in Negroes. Melanoma of the optic disc must be differentiated from congenital melanosis and from pigment deposits about and on the disc when they are of no particular significance. It is noteworthy that in no instance has a melanoma of the optic disc or nerve been known to metastasize. It is questionable that a melanoma of the optic nerve can ever be properly termed as malignant (fig. 1).

Gliomas. These occur more frequently than any other intrinsic optic nerve tumor (fig. 2). In our series most of these tumors were astrocytomas but two were thought to be oligodendrogliomas.

Meningiomas. These tumors may affect the optic nerves, both within the orbit and intracranially, and they may involve the chiasm. Until a few years ago it was debated as to whether such tumors ever remained entirely confined to the orbit. Dr. Jonas Friedenwald observed one such case, and Dr. Lorenz Zimmerman has available several specimens of purely orbital meningiomas in the Armed Forces Institute of Pathology. In this paper there is presented in summary form what has seemed to us an important example of meningioma involving the optic nerves and chiasm (K. H. 127591).

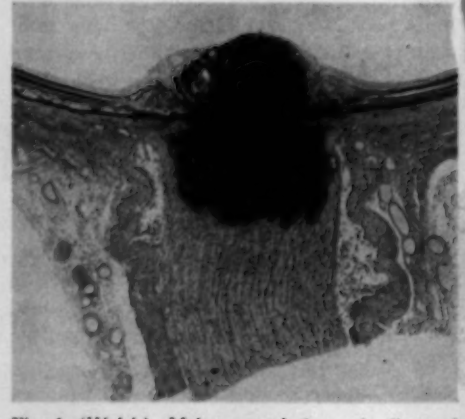


Fig. 1 (Walsh). Melanoma of the optic disc and nerve. (Dr. Eubank. AFIP Acc. 507852.)

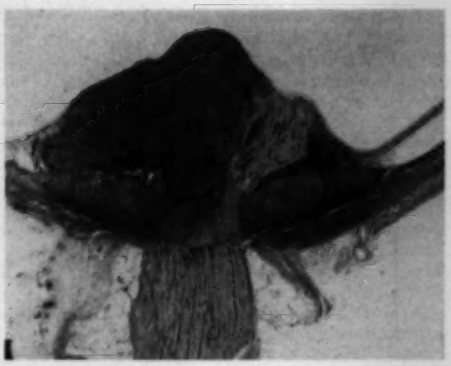


Fig. 2 (Walsh). Malignant melanoma of the choroid, involving the optic disc.

Angiomas. Angiomas and vascular tumors may involve the optic disc. No such case is included in this series. Wyburn-Mason described such tumors as visible at the nerve-head and extending along the optic nerve to the brainstem and associated with fits. I have been on the lookout for such a case but have not yet encountered one.

Neurofibromas. In our series one case was reported as a neurofibroma of the optic chiasm and in another case neurofibroma of the optic nerve. Such a diagnosis raises an interesting problem.

Neurofibromas involving the peripheral nerves arise from the sheath of Schwann. The optic nerves and the chiasm do not have any sheath of Schwann. It would seem to follow that neurofibroma of the optic nerve or chiasm is an untenable diagnosis. This conclusion is not necessarily correct.

It has been suggested by Penfield and by Hortega that Schwann cells and oligodendroglial cells are essentially similar in that either may elaborate and maintain myelin sheaths. According to Hortega the tumor in the optic nerve is essentially an oligodendrocytoma (see Reese).

Davis, who has stressed the occurrence of tumors of the optic nerve and chiasm as being often associated with von Recklinghausen's disease elsewhere, has studied so-called neurofibromas of the optic nerve carefully. He has concluded that such tumors of the optic nerve and chiasm as may be associated with neurofibromas are either gliomas or endotheliomas (meningiomas). He did not entirely disregard the possibility of there being present in some instances a true neurofibroma when he remarked: "It is possible that the finer branches of the peripheral or sympathetic nerves which enter the optic nerve stem with the blood vessels (Salzmann) along the pial invagination might be subject to neurofibromatosis in its strictest sense."

Metastatic carcinoma. We have observed only one metastatic carcinoma which seemingly affects the optic nerve. Through the courtesy of Dr. Zimmerman we are able to observe an interesting microphotograph of such a case (fig. 3).

Ocular symptomatology

Tumors involving the optic disc. In three individuals the ophthalmoscope revealed what seemed to be tumor of the optic disc. One of these patients (L. S. 11943—FBW) was seen through the courtesy of W. M. Boles (fig. 4). The visual acuity of the affected left eye was 20/50. A gray mass seemed to originate from the nasal side of the optic disc. It seemed possible that the tumor had extended into the nerve from the adjacent retina. After several months' ob-

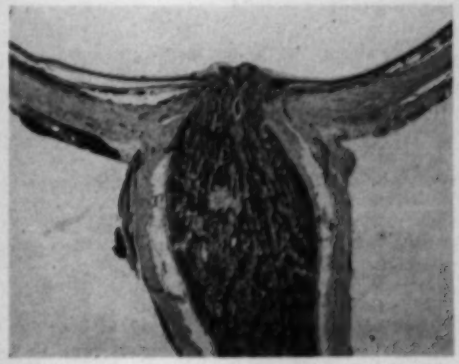


Fig. 3 (Walsh). Metastatic carcinoma from the breast. (AFIP Acc. 57689, McDanald and Payne.)

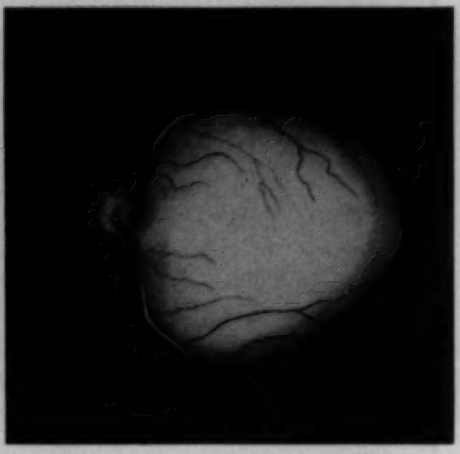


Fig. 4 (Walsh). Glioma of the optic disc in a young girl. (Courtesy of Dr. W. M. Boles.)

servation the visual acuity had become progressively defective. The eye was enucleated and the tumor was found to be an astrocytoma originating in the optic nerve.

In another patient a mass protruded from the disc. Since the patient suffered from cancer of the breast, it was thought that the optic nerve tumor was metastatic cancer (A. E. 164361). In another patient (K. H. 127591), whose case is summarized below, it was recognized, when he was 11 years of age, that there was a tumor which probably originated in the right optic disc; 17 years later it was shown that the tumor was a meningioma.

Case 1

History. An 11-year-old white boy had a blind right eye, with optic atrophy on right. A mass protruded from the right optic disc. Enucleation of right eye was advised but was not done. The left eye was normal. Seventeen years later there was defective vision in the left eye and loss of temporal field. The right eye was enucleated. There was extensive tumor invasion of the nerve and choroid about the optic nerve. Craniotomy revealed a tumor of the right nerve intracranially and of the chiasm and left optic nerve.

Original examination. K. H. (127591) was reported to have had loss of vision not associated with pain and affecting the right eye over a period of three weeks when he was first seen. The right eye was blind. It diverged five to 10 degrees and so, probably, had been blind for a longer time than stated. There was an irregular swelling of the optic disc; it measured three diopters and extended into and merged with the adjacent retina. The abnormal area was estimated to be five times the size of the disc. X-ray studies of the optic foramina showed nothing remarkable. The floor of the right orbit was slightly irregular and the right antrum was cloudy. Tumor, optic neuritis, and congenital anomaly were considered as possible diagnoses. Finally enucleation was advised. The patient failed to return for operation and was not seen again until 17 years had passed.

Present examination. Fifteen years after his first examination the vision of the left eye became defective. Within 18 months he was unable to read. Five weeks before his return visit he stopped work as a truck driver. He complained of mild frontal headaches in addition to loss of vision.

Examination of the eyes revealed no change in the blind divergent eye, both as regards position and ophthalmoscopic appearance. The vision of the left eye could be corrected to 20/40 — 1. The left disc was pale and the nasal side of the disc was slightly elevated. Almost the entire temporal field was lost. There was a mild right divergent strabismus but both eyes moved freely and fully. There was no exophthalmos.

X-ray studies of the optic foramina showed the right to be slightly larger than the left (6:4.5 mm.). There was slight erosion of the right superior orbital margin and greater wing of the sphenoid.

The right eye was enucleated. The stem of the nerve was greatly enlarged and was firm when cut.

Sections showed the tumor to be a psammomatous meningioma involving the choroid about the optic disc and invading the nerve as well as producing great thickening of the dural sheaths of the nerve.

Operation. A week later a craniotomy was performed (Dr. George Smith). The right nerve was greatly thickened and incorporated in a mass of tissue which involved the sphenoid ridge. The chiasm was thickened as was also the left optic nerve at its junction with the chiasm. Sections of the right optic nerve again revealed psammomatous meningioma.

Two months after operation the vision of the left eye was 20/70 — 1. The appearance of the disc was unchanged.

Comment. Remarkable features of this case were: unchanged appearance of the right eye over a period of 17 years; the slow growth of the tumor as evidenced by the vision of the left eye remaining unaffected for 15 years; the lack of proptosis; the absence of ophthalmoplegia; the normalcy or rather slight widening of the optic canal of the right eye (Fig. 5). This case will be reported subsequently by Dr. Shephard N. Dunn.

As regards *vascular tumors* involving the optic disc, we have not seen any case justi-

fying extended comment. However, brief mention is made of a case which seems to qualify. S. P. 461580, a young adult white male, suffered from angiomatosis of the retina—an angioma almost touched the optic disc. In addition, he had an angioma of the spinal cord. Several members of his family suffered from angiomatosis, as has been recorded by Silver and Henningar.

Defective vision. In 17 of 25 cases, vision was defective at the time of first examination. In seven individuals the defect was bilateral. In one patient (K. H., Case 1 summarized above) the second eye was ultimately affected. The defect in vision did not follow any pattern in these cases. In seven individuals, defective vision was known to be present for less than a year when we first saw the patients. Ten individuals had had defective vision for more than a year when we first saw them.

In one patient (L. S. 11943-FBW) the tumor of the optic disc, a proven glioma, was found on routine examination of the eyes of a six-year-old child about to commence school. Certainly, in such an instance, differentiation from some type of congenital anomaly posed a real problem. Demonstration of further loss of vision was the deciding factor in enucleation of the eye.

In another patient, complaint of headaches and poor nutrition resulted in a suspicion of anorexia nervosa in a five-year-old child. Further examination revealed bilateral papilledema and hydrocephalus; there was erosion of the posterior clinoids; a ventriculogram showed lack of filling of the third ventricle. A Torkildsen procedure was carried out. Later an exploratory operation showed tumor of the chiasm with extension into the third ventricle. Much of the tumor was removed; it was an astrocytoma. The papilledema disappeared and there was said to have been improvement in vision (S. B. B13319).

Another child, a boy aged four years (C. C. A03084), was examined because of the development of a left hemiplegia of eight months' duration. At exploratory operation he was found to have a glioma of the chiasm. Vision was 6/15 and 5/10 in the right and left eyes respectively. Death occurred a month after operation.

A white girl, 22 months of age (I. G. 706792), was brought to the ophthalmologist because of a squint and some proptosis of

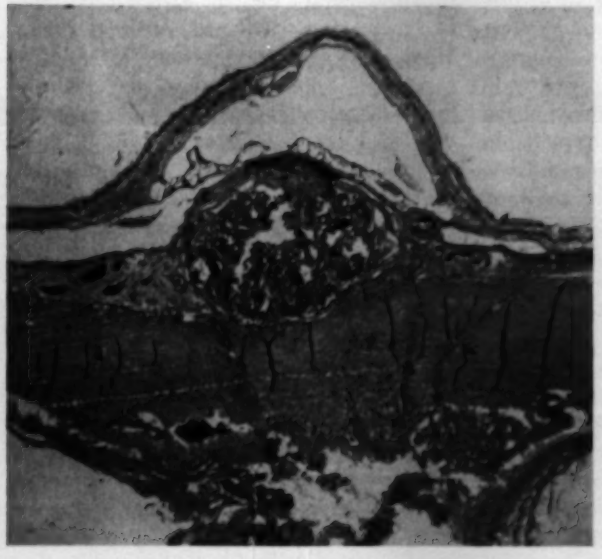


Fig. 5 (Walsh). Intraocular meningioma. (K. H. 127591.) The tumor involved the optic nerve and chiasm.

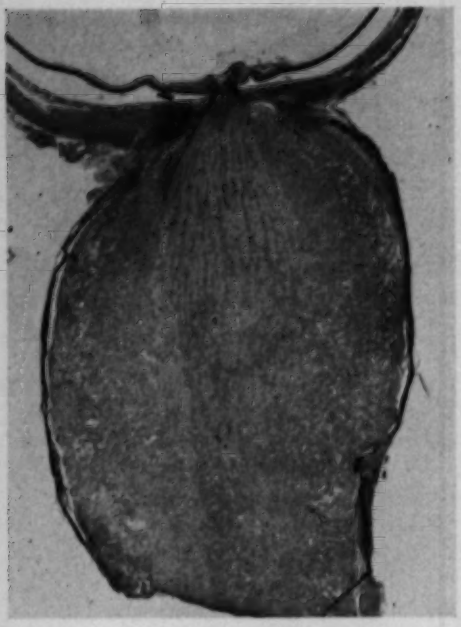


Fig. 6 (Walsh). Glioma of the optic nerve. (AFIP Acc. 269268.)

the squinting eye. Ultimately she was found to have a glioma of the nerve (fig. 6).

Proptosis. This was present in 10 of 25 cases. The most pronounced proptosis amounted to 15 mm., present in greatest part for eight years; the vision in the proptosed eye was 20/70. Mention has already been made of K. H., with meningioma of the optic nerve, present for 17 years, with no proptosis, in spite of there being a large tumor within the orbit. In three cases of tumor of the chiasm, there was proptosis of only one eye. In two of these individuals, it was found at operation that the tumor had extended forward into the orbit producing the proptosis.

Our experiences with proptosis have suggested: (1) It is not necessarily present when there is a tumor involving the optic nerve within the orbit; (2) the amount is variable; (3) the eye may be shoved straight forward or it may be displaced in any direction—usually there is some downward displacement; (4) it is impossible to correlate the type of intrinsic nerve tumor and the amount of proptosis.

Ophthalmoplegias and position of the eyes. We are unhappy with our records in these regards. In several cases of tumor of the chiasm, the eye position and ocular movements were quite normal. This also was the case with tumors involving the optic disc and in some cases of orbital optic-nerve tumor. In one individual prior to operation, there was complete immobility of the eye. After operation, particularly when a craniotomy was performed, total ophthalmoplegia with ptosis was present in several instances. Defective power in elevating the eyes was more common than any other. In several instances abduction only was defective.

Nystagmus. This was present in three individuals who were shown to have a chiasmal tumor. All were children. In all of these patients, the nystagmus was vertical. In the first two seen there was tumor of the chiasm and extension to adjacent structure. Both patients died after operation (A. R. 46310, R. S. 593800). The third member of this group, a 21-month-old white child (G. H. 498970; A69689), had pale discs and vertical nystagmus. On the basis of the other two cases, we suspected chiasmal tumor. However, there was a history of exposure to methyl alcohol and it was suggested that the optic atrophy and nystagmus might be due to alcohol intoxication. Exploratory operation revealed tumor filling the third ventricle and invading the chiasm (astrocytoma). The child died several weeks after operation. These three cases were studied at about the same time. They suggested to us that, in a child, loss of vision and vertical nystagmus strongly suggest chiasmal tumor with involvement of adjacent structures. Furthermore, in such cases the outlook is decidedly poor.

Optic atrophy. Pallor of the optic discs with reduction of visual acuity was present in 18 instances; it was bilateral in 11 persons.

Papilledema. This was present unilaterally in six and bilaterally in one patient. There was optic atrophy in one eye and papilledema in the other in a single individual (W. C. 311305).

Visual field defects. With intrinsic tumors of the optic nerve or chiasm it may be impossible to chart defects because of the youth of the patients. The field defects with optic nerve tumors vary within wide limits and there is no characteristic defect. With tumors involving the chiasm the field defect is characteristically bitemporal if the chiasm is first affected. We have observed central scotomas, irregular unilateral and bilateral defects, homonymous and bitemporal hemianopsia with chiasmal involvement. Bitemporal defects, usually with optic atrophy, should suggest the possibility of tumor. In children with anteriorly situated tumors we have seen temporal defects of the visual fields in six of 12 patients less than 21 years of age with craniopharyngiomas, with intrinsic chiasmal tumors in five of 19 patients under 21 years of age, and with pituitary adenomas in two of six patients under 16 years of age.

Evidences of neurofibromatosis. In our series of cases there were four patients who exhibited evidences of neurofibromatosis. One of these (E. C. 133821) had generalized neurofibromatosis and exhibited bitemporal field defects and bilateral optic atrophy. Almost certainly there was a chiasmal tumor present but operative therapy was refused.

Davis, whose work regarding optic nerve and chiasmal tumors in association with von Recklinghausen's disease is well known, remarked upon the infrequency with which generalized and extensive neurofibromatosis is associated with involvement of the optic pathways. Our case, just cited, offered an exception to this generalization.

In three other patients there were cafe-au-lait patches which suggested that the involvement of the optic pathways might be the result of glioma. It is always possible that cafe-au-lait spots were present and missed in individuals in this series but I have been aware of the association for many years and am doubtful that such is the case.

We observed evidence of neurofibromatosis in four of 26 patients, an incidence of 15.4 percent. Marshall found evidence of von Recklinghausen's disease in 108 of 660 primary tumors of the optic nerve from the literature and personal observation, an incidence of 16.4 percent. He expressed belief that, if there were present at least six cafe-au-lait spots of at least 15 mm. in diameter, there is unquestionable evidence of neurofibromatosis. Dr. Davis feels that Marshall's figure of 16 percent and mine of 15 percent probably do not represent the full percentage chance of tumor of the nerve or chiasm being associated with or part of neurofibromatosis. I am inclined to agree.

X-ray evidence of optic nerve tumors. The most important single X-ray finding in these cases of intrinsic optic nerve tumor is enlargement of the optic canal. A pronounced disparity in the size of one canal to its probably normal fellow is more important than increased size alone (Carroll quoting Pfeiffer). A canal up to seven mm. in size may be normal. There may or may not be erosion of the canal when tumor is present. In our 25 cases the optic canal was enlarged in nine.

It is important to recognize that optic-nerve tumor within the orbit may be associated with tumor involving the intracranial nerve and yet the optic canal may be enlarged only slightly (see Case K. H. already summarized). Unquestionably absence of change in the optic canal does not invariably mean that tumor has not extended via the canal to within the cranium.

A combination of optic atrophy with poor vision and a dilated optic canal as compared with the canal of the opposite side almost certainly indicates optic-nerve tumor. We observed this situation in a girl (B. G. 11658-FBW), aged seven years. The defective vision was found on routine examination. The possibility of there being a congenital

Fig. 7 (Walsh). Coloboma of the optic disc. Massive gliosis of the optic disc. Pseudotumor. (Dr. A. M. Culler. AFIP Acc. 211587.)

condition seemed unlikely in view of the fact that with an undeveloped optic nerve there should be narrowing of the optic canal. The canal measured seven mm.; its opposite measured four mm. I advised operative intervention in this case. The parents did not consent to operation.

Differential diagnosis intrinsic tumors optic nerve and chiasm

Appearance of optic disc. In Figures 7 and 8, shown here, it is obvious that, with the ophthalmoscope alone, it may be quite impossible to differentiate between a developmental anomaly, long-standing inflammatory involvement, and tumor of the optic disc. Optic atrophy, papilledema, or optic neuritis may result from intrinsic nerve tumor.

Visual loss. There is nothing characteristic about the loss of vision to indicate intrinsic nerve or chiasmal tumor. A history of sudden loss of vision always suggests optic neuritis, but individuals who suffer from intrinsic tumor may describe sudden loss of vision when really they had failed to notice long-standing loss.

Again as regards optic neuritis we have had central scotomas in proven cases of tumor. It seems probable that "hard" tumors which have extended into the orbit, as, for example, meningiomas originating on the sphenoid ridge, produce less loss of vision than do "soft" tumors, such as hemangiomas involving the orbit.

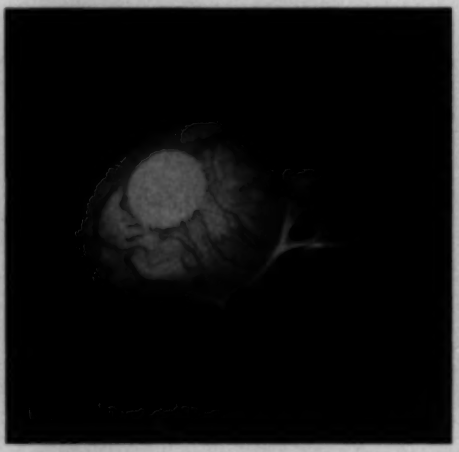


Fig. 8 (Walsh). Developmental (?) anomaly at disc in the eye of a 13-year-old boy. (Courtesy Dr. E. Burton.)

Loss of vision due to macular involvement not visible with the ophthalmoscope should be remembered as a possibility in some of the problem cases. In one instance, ridging of the retina in the macula in an individual who had slight loss of central vision and questionable proptosis raised a problem in diagnosis. Exploratory operation revealed a hemangioma. When the onset of visual loss is sudden it is unlikely that a tumor is present.

"Ridging" of the retina. When ridging is an isolated finding involving the posterior pole of the eye, in our experience, it has invariably meant that a mass is pressing into the posterior aspect of the eyeball, providing that the disc appearance is quite normal. If the disc is or has been swollen, ridging may be due to traction.

Visual field defects. Any type of field defect may originate in orbital optic-nerve tumor. The nature of the field defect is important when the second eye is involved or when there is chiasmal involvement.

Palpation. With intrinsic tumors of the optic nerves and chiasm, the orbital margin usually seems normal. However, with intrinsic tumor on three occasions, we have palpated a mass in the orbit (L. K. A23565; B. M. 560586; T. K. 396799). Pulsation may be felt and a bruit may be heard when there is proptosis and transmitted pulsation from a vascular abnormality (carotid cavernous fistula or other arteriovenous fistula) or from cerebral pulsation when there is a defect in the orbital roof.

Intermittent exophthalmos. This is not a feature of intrinsic optic-nerve tumors. It may occur with hemangioma of the orbit, as observed by Dr. E. A. Walker. As has been shown (Walsh and Dandy), such cases may be explained on the basis of intracranial vascular abnormalities within the cranium.

Proptosis. It has been generally thought that intrinsic nerve tumors are likely to push the eye straight forward. With an eye in this position intrinsic tumor is a real probability, but the proptosis may be in any direction with such tumors. With so-called malignant exophthalmos the relatively narrow palpebral fissures, swollen eyelids, and increased orbital tension should be recalled; also the fact that metastatic orbital tumors are likely to produce what would seem to be an inflammatory state. Again, proptosis is not essential to the diagnosis of orbital tumor.

Ophthalmoplegia. It is impossible to differentiate between intrinsic optic nerve tumors and extrinsic orbital tumor on the nature or extent of the ophthalmoplegia. We have observed cases of pseudotumor of the orbit in which there was extreme displacement of the eyeball. It seemed reasonable in several such instances to visualize direct infiltration of ocular muscle as the explanation for the displacement.

X-ray findings. These are not further mentioned here.

Biopsy and laboratory findings. Brief mention is made of several significant laboratory findings. With orbital tumors such as eosinophilic granuloma there is likely to be eosinophilia; this applies to orbital parasitic involvements.

Biopsy is often the deciding factor. It should be deferred until all ordinary examinations are made.

With children it is always necessary first to consider metastatic tumor of the adrenal so that pyelograms are in order on almost every child who exhibits proptosis.

Treatment of orbital and of intrinsic tumors of optic nerve and chiasm.

This subject invariably produces vigorous disagreement among ophthalmologists. Only in a few instances have neurosurgeons advocated their services in dealing with orbital tumors; for the most part these colleagues stand by available and pleased to operate transcranially if requested to do so. What is contained in this section represents what seems a reasonable attitude. What is the best possible handling of a problem in one center might not represent the most efficient method in another (Table 2).

TABLE 2

TREATMENT INTRINSIC TUMORS

	Chiasm	Optic Nerve
Craniotomy and biopsy	13[a]	1[b]
Decompression optic canal and orbital roof	2[c]	4[d]
Enucleation	1[e]	3[f]
Exenteration		1[g]
Krönlein		1[i]
Radiation, postoperative	6[j]	1[h]

[a] C. C. A93084—R. S. 593800—M. E. G. A93531—B. R. 4734(FBW)—G. H. A69689 & 498970—M. H. 414406—R. R. A46310—L. M. G. 130317—W. S. (Church Home)—S. B. B13319—S. W. B13803—B. D. 438415—J. H. 708572.
[b] J. R. 523114.
[c] K. H. 127591—W. C. 311305.
[d] I. G. 706792—P. H. 405501—C. G. 606646—L. K. A23565.
[e] K. H. 127591.
[f] B. M. 560586—L. S. 11943 (FBW)—L. K. A23565.
[g] T. K. 396799.
[h] P. H. 405501.
[i] M. E. G. A93531—M. H. 414406—S. W. B13803—S. B. B13319—W. S. (Church Home)—V. D. 438415.
[j] C. G. 606646.

X-ray therapy is indicated in a minority of cases. If tumor of the chiasm has been established, rotentgen-ray therapy is indicated. Removal of the chiasm is contraindicated on two scores: immediate and total blindness and danger to life.

We have notes on two patients who suffered from tumor of the chiasm and who were treated with X-rays. This therapy helped materially, although admittedly it is difficult to evaluate results of therapy in slow-growing tumor of the chiasm:

M.G. A93531, a child aged four years, exhibited several cafe-au-lait spots and defective vision; it was established that she had a glioma of the optic chiasm. After three years, she remained able to distinguish large objects with either eye (child also was seen by Dr. F. A. Davis). In this patient two courses of therapy were given (usually 4,000 r is the dosage).

A child, aged seven and one-half years, who had a tumor of the chiasm said to be an oligodendroglioma, had 5/200 and 20/70 vision in the right and left eyes, respectively; six months after X-ray therapy there was no demonstrable change in the visual status.

As regards obtaining of biopsy material, we have been surprised to read a brief Society Transaction communicated by Taveras, Wood, and Mount, who seemingly based their ideas on 34 patients with optic nerve gliomas (and chiasm) treated at the Neurological Institute of New York and the Institute of Ophthalmology. They were agreed that X-ray therapy is important in the treatment in of these intrinsic tumors and remarked that, in some instances, exophthalmos had receded completely as a result of such therapy. Surgery, other than exploration, should be reserved for cases in which there is an obstruction to the flow of the cerebrospinal fluid or in which exophthalmos has failed to respond to radiation therapy. Mount insisted that, if the optic nerve or chiasm is found to contain a tumor, no biopsy tissue should be removed for examination. He remarked that in one case he performed a biopsy on a child, eight years of age, and now the only visual impairment, he believes, is the result of the biopsy. While this viewpoint may ultimately receive wide acceptance, it seems unreasonable to me.

The following generalizations regarding surgical procedures on orbital and optic-nerve and chiasmal tumors have seemed reasonable in the light of our experience.

1. It is impossible to generalize as to when operation should or should not be performed because cases vary within wide

limits. However, it should be borne in mind that, excepting in the instance of retinoblastomas, operative removal of orbital tumors is rarely a life-saving procedure. Often it is a sight-saving effort.

2. If it is thought that the tumor is contained within the orbit, it can be removed by the ophthalmic surgeon through a classical Krönlein procedure or some modification of it. If it is recognized that the tumor is within the optic nerve, it is proper to obtain biopsy tissue. If the tumor is a glioma, radiation may suffice to arrest the progress and cure the patient. If, in such an instance, the visual acuity is already lost or is extremely low, removal of the swollen segment of nerve may suffice and would be the method of choice. If the tumor is far posterior in the orbit, unless there is reason to believe that it has extended into the cranial cavity, removal and roentgen-ray therapy is indicated, if the section shows glioma.

This represents in some degree a change in the beliefs of one of us (FBW).

3. If the tumor is thought to be entirely within the cranium, the neurosurgeon should undertake the operative treatment.

4. If the tumor is thought to be both intracranial and intraorbital (and this is always the case if the optic canal is dilated), operation should be transcranial. The situation calls for combined efforts and the ophthalmic surgeon may be of great assistance when the orbit has been unroofed.

5. It is the neurosurgeon's responsibility if, after a transcranial operation has been performed an enucleation or exenteration of the orbit is required, that the cerebrum does not herniate into the orbit. Limited unroofing of the orbit gives an unsatisfactory approach to the orbital contents. Insertion of a tantalum plate or some such maneuver is necessary after the orbit has been unroofed.

Several cases are now mentioned. In L. K. A23565, a transcranial approach was made for a tumor which was strictly within the orbit. The tumor was a meningioma. Following operation there was great protrusion of the eye, with displacement and pulsation. Undoubtedly there was prolapse of the frontal lobe through the orbital defect.

In another case, reported by Dr. A. B. King, such a prolapse occurred. It was remedied after several operations which included insertion of a tantalum plate over the defect in the orbital roof.

After a Krönlein type of operation in the case of P. H. 405501, for what was said to be a meningioma affecting the optic nerve, there was, six months later, a development of third-nerve paralysis and involvement of the first and second divisions of the fifth nerve. It was thought there had been extension of the tumor and a transcranial operation failed to reveal any intracranial extension of the tumor but additional tumor tissue was removed from the apex of the orbit. In this case there was no enlargement of the optic canal.

An unusual complication as regards the eye on the side of operation is now described:

Case 2

The left eye of W. C. 311305 was proptosed and it deviated down and out. The left optic canal was 10 times the size of the right canal.

A tarsorrhaphy was done on the left. Then a craniotomy was performed and the roof of the orbit was partially removed. A section of the orbital optic nerve was removed. The tumor (total weight 12 gm.) was said to be a neurofibroma.

Following operation there was increased proptosis of the left eye with pulsation and loss of the temporal field in the right eye. Dr. Jack Guyton drew attention to the deep anterior chamber in the left eye at the time of the first dressing. The iris was "tented" backward and the eye was very soft. It seemed probable to Dr. Guyton (and to us) that the optic nerve had been avulsed at the time of operation or, when it was severed, the posterior part of the eyeball had been opened. Nine years later this patient had a few convulsions. A later communication stated that he was quite well.

II. Extrinsic tumors affecting the optic nerves and chiasm

In this section both orbital and intracranial tumors are considered. Clinical features are described in summary form, and little or no attention is given to the microscopic diagnosis of these tumors.

MENINGIOMAS

We have studied 31 patients shown to have a meningioma involving the optic chiasm or the optic pathways anterior to the chiasm. It is of ophthalmologic interest that the diagnosis of these tumors in the situations mentioned is principally dependent upon the ocular symptomatology.

Loss of vision in one eye was present in 17 instances; in eight there was profound loss of vision in both eyes; in four the loss of vision in both eyes was slight and in two there was good vision bilaterally.

Optic atrophy was ophthalmoscopically visible in 18; in 10 there was bilateral optic atrophy; in two individuals the optic atrophy was "secondary."

Papilledema was present bilaterally in one case; in two there was papilledema on one side and optic atrophy on the other side; in two secondary atrophy developed after papilledema.

Proptosis was present in five individuals affecting one eye. It was not pronounced in any case in this group. In one patient there was present both a meningioma and a hemangioma of the orbit (B. E. 465456).

Visual field changes were present in 29 of the 31 cases. Further information as regards these findings is included in the following paragraphs dealing with tumors in specific areas.

OLFACTORY-GROOVE MENINGIOMAS. Among seven such cases three were bilateral. Anosmia was present in four. Loss of vision was pronounced in five patients (six eyes). Optic atrophy was visible in six. Papilledema was present in two individuals and it was bilateral. In one individual the fields were normal excepting for enlargement of the blind-spots (G. Y. 592418). In one there was a right upper homonymous defect (H. J. 557486). Bitemporal defects were present in two patients (in one field there was also a central scotoma) (M. W. 415998; E. B. 505045). In three cases there were central field defects (A. A. 464088; E. H. 597612; A. R. 425618). We did not have a good example of Gowers-Foster Kennedy syndrome in this group. Cranial-nerve palsies seemed noteworthy by their absence according to my notes but certainly some such were present.

One remarkable case summary is presented and several interesting cases are mentioned briefly. It exemplifies what seemed to me to be remarkable astuteness on the part of the patient's physician for reasons outlined below. It represents the occurrence of two disease entities in one individual.

CASE 3

History. A Negro teacher, a man, aged 46 years, had defective vision bilaterally. Vision was: R.E., 20/40; L.E., 20/50. Diagnosis was made of general paresis supported by serologic findings and clinical observation. There was a history of treatment for syphilis 11 years earlier. A questionable right upper homonymous field defect was present. The syphilologist suggested that tumor rather than syphilis produced the optic atrophy. Malaria therapy had been given. There was bilateral anosmia. The olfactory-groove tumors were removed at operation, with recovery.

H. J. (557486) suffered from general paresis and examinations were made with difficulty. The physician responsible for his care suggested that the visual acuity was better than would be anticipated if syphilitic optic atrophy were responsible for the visual defects. He thought from the onset that tumor was present. Treatment for the paresis consisted of administration of penicillin, also malaria therapy. It was shown that bilateral anosmia was present. Olfactory groove meningiomas were removed, one from each side. Two years later there was recurrence on one side and reoperation was done. Final vision was: R.E., counts fingers; L.E., 20/30.

CASE 4

History. A 51-year-old white woman had bilateral olfactory-groove meningiomas. Vision was: R.E., counts fingers; L.E., 20/50. There were bilateral central scotomas, bilateral optic atrophy, bilateral anosmia. The interesting fundus findings were unexplained.

E. H. (597612) exhibited ophthalmoscopically visible optic atrophy and the fields contained central scotomas. There were folds in the macular region of the right eye so that it was thought there might be a small mass in the orbit. There was no proptosis.

At operation there was no extension into the orbit, so that we have no explanation for the retinal folds which persisted during the time she was under our observation.

An individual who had had defective

vision in one eye for seven years and in the other eye for three years had an olfactory-groove tumor which affected both sides; also she had had polyuria and polydipsia for several months (E. B. 505045). Another olfactory-groove tumor patient had amenorrhea. (A. R. 425618).

OTHER MENINGIOMAS. We have studied 22 individuals with meningiomas other than those originating in the olfactory groove. In all the meningiomas under consideration ocular signs are predominant but, in our cases, the symptomatology was that which is described in standard textbooks. In consequence this section is shortened to include a paragraph on the ocular symptomatology encountered and brief mention of interesting features of several cases. Our material concerns meningiomas arising from the frontal lobe, the tuberculum sella, the sphenoidal ridge, and the falx and parasagittal region.

Meningiomas which originate from the frontal lobe are likely to have the symptomatology of olfactory-groove tumors. Those arising from the tuberculum sella may be associated with third-nerve palsy but are more often characterized by bitemporal field defects. Such suprasellar tumors, also others which are above the sella, often produce what Cushing described years ago: primary optic atrophy with bitemporal field defects in adult patients with essentially normal sella turcica.

Meningiomas arising from the inner third of the sphenoid ridge are likely to produce at first a unilateral optic atrophy. Such tumors are particularly likely to be labelled as optic neuritis in the early stages. It is in such cases that a Gowers-Foster Kennedy syndrome may originate (although I personally have had little experience with this syndrome in pure culture). After a time other signs develop: ocular muscle palsies and involvement of the temporal field of the opposite eye.

Middle ridge tumors in their early stages are characterized by a lack of eye signs. Later there is loss of vision, optic atrophy, and homonymous field defects. Outer ridge tumors are characterized by exophthalmos in many instances. Usually there is a palpable mass in the temporal fossa and there is late loss of vision.

Parasagittal meningiomas which originate along the superior sagittal sinus produce Jacksonian convulsions and rather often a slowly progressive hemiplegia or heminanesthesia. In some cases there may be aphasia. Papilledema, visual hallucinations, and optic atrophy develop when the tumor has been present for some time.

Meningiomas may be multiple. In one patient three meningiomas were identified (A. G. 633348). One originated from the left frontal area and one from the falx and one below the left optic nerve; there was bilateral optic atrophy and, postoperatively, a pituitary insufficiency.

Another example of multiple tumors was B. E. (465456) who was found to have a sphenoidal ridge meningioma and a cavernous hemangioma of the right orbit. Further interest in this case centered on her complaint of misshapen objects, metamorphopsia, in the right eye; the field of the defective eye contained a ring scotoma. The patient died and was found to have suffered a softening of the right hemisphere.

In another patient, F. A. (646858), there was proof of the existence of lymphogranuloma inguinale; he was shown to have a meningioma of the tuberculum sella; there was macular edema bilaterally although the left disc was normal and there was questionable change in the left disc.

A left frontal lobe meningioma was responsible for amenorrhea in M. S. (1518 FBW). F. A. (CEI 8571) was found to have two meningiomas, one arising from the falx and the other at the base. The right eye was proptosed for 30 years and was blind and painful. The left eye remained normal.

Fincher's interesting paper on "Experiences with Meningiomas" deals with multiple tumors. His Case 1 concerns a meningioma which may have been produced by surgery;

a meningioma developed at the site from which an astrocytoma had been removed many years earlier.

A. R. (425618), an adult woman with an interpeduncular meningioma, which originated in an olfactory groove, had amenorrhea and a central scotoma in her better eye; the other eye was blind.

Mention is made of an individual whose bilateral optic atrophy and central scotomas and family history led me to make a diagnosis of Leber's optic atrophy. This individual's visual acuity was 20/200, approximately. The vision failed further 10 years after I had seen the patient and, at operation, a large suprasellar meningioma was removed.

In a woman with syphilis and mental retardation, both eyes were blind. There was optic atrophy in one eye and papilledema in the other. At operation a meningioma was found in a parahypophyseal position extending into the third ventricle; the left optic nerve (the atrophic nerve) was encased in tumor.

Craniopharyngiomas

We observed 23 patients suffering from craniopharyngioma. The sex incidence was nearly equal, 12 males and 11 females. The youngest patient was aged two years, the oldest, 62 years (J. T. 434205; M. G. 2265 CEI). Nine of the 23 patients were less than 21 years of age. Five patients were over 50 years of age when found to have tumor. (A recent report by Witt, McCarthy, and Keating concerns two patients over 60 years with craniopharyngioma. They found reports on only five patients more than 60 years of age.) Twelve had no evidence of pituitary dysfunction. Diabetes insipidus was present in four patients (R. P. 511188; D. R. 379576; T. W. 13991-FBW; M. G. 2265 CEI). Lack of sexual development was a prominent feature in two individuals (N. A. A69696; C. G. A91456). Acromegaly was present in one (D. R. 379576). Obesity was present in one (P. P. 614236). Amenorrhea was present in one (M. D. 4013-CEI).

Visual loss was not a feature in four patients all of whom exhibited normal optic discs (B. K. 474263; V. E. 106458; C. P. 453920; G. B. 553218). One such patient had a bitemporal field defect (C. P. 453920). Of 17 patients who had visual loss it was bitemporal in 10 and unilateral in seven. Optic atrophy was present as visible with the ophthalmoscope in nine cases of bilateral involvement. In one case atrophy was secondary to a papilledema (H. A. A69696). Papilledema was present in both eyes of three individuals (R. B. 703485; J. N. A29062; B. K. 474263).

It has seemed particularly important to us that, with craniopharyngioma, the optic discs may appear entirely normal with the ophthalmoscope in the presence of long-continued defect in vision or in the visual fields (R. P. 511188; V. E. 106458-Mercy; C. P. 453920; M. D. 4013-CEI; R. P. 7205-FBW). We have observed this more often with craniopharyngioma than with any other type of tumor. It would seem reasonable at this time to make what we consider an important diagnostic generalization. If there is loss of vision and the loss has been present for two or three or more months and the optic discs appear normal, tumor and not optic neuritis is the diagnosis of choice.

Bitemporal field defects were present in 11 of these patients so that it can be considered as the typical field defect in such cases. Homonymous field defects were present in two individuals (R. P. 511186 and G. I. 462309). In T. W. (13991-FBW) there was nasal defect in the field of one eye and peripheral narrowing in the other field. Central scotomas were present in three cases (P. P. 614236; M. G. 2265-CEI; E. S. 420674).

Roentgenograms of the skull failed to reveal any abnormality in six patients. Calcification above the sella was a frequent finding. The sella was enlarged in five individuals and the clinoids were eroded in five. In one there was a thickening of the sphenoidal ridge and a defect in the left frontal sinus.

Recurrence of the tumor occurred in four patients. One of these died and at autopsy it was shown that there was herniation of both uncinate gyri and there was a huge residual tumor.

Surgical procedures were carried out in all 23 cases. Craniotomies usually were performed through the hypophyseal approach. Cysts were evacuated in most instances. In no case was a total removal attempted although in several the operator thought that possibly all the tumor has been removed. Reoperation was undertaken for recurrence in three instances. Roentgen-ray therapy has been advocated for recurrence and routinely after operative intervention. We have advised it under such circumstances.

Experiences with craniopharyngiomas have been to me most interesting. Mention has already been made of there frequently being normal-looking discs when there has been long-standing loss of vision and changes in the visual fields. Such a combination now suggests the possibility of craniopharyngioma to me. Several cases are now cited for their individual interest.

Case 5

History. A child, 18 months of age, was thought to have defective vision in both eyes. The possibility of tumor was considered. A short history suggested the possibility of bilateral optic neuritis. A delay in examination seemed reasonable. An apparent improvement in vision was reported. Two years later, the child returned blind and with hydrocephalus.

J. T. 43205 was seen through the courtesy of Dr. Blair. The apparent defect had been present for two weeks according to the parents. There was no definite history of any recent illness.

Examination of the eyes showed them to be normal externally save for wide pupils which reacted scarcely at all to light. The optic discs were questionably pale for a blond child. X-ray examinations gave normal findings.

It was thought that, since the child might have an optic neuritis, spinal air might be delayed. The child was discharged to its home. Three weeks later a letter from the referring physician stated that the visual acuity of both eyes had improved so that the child picked up the smallest objects from the floor. It seemed that our conservative handling of the case had merit.

Two years later the child was seen again. There was pronounced hydrocephalus. The optic discs were atrophic and the visual acuity was essentially nil. Operation revealed a craniopharyngioma.

The case just cited shows that visual loss does not always progress when a cerebral tumor is present. The vision may improve. With a craniopharyngioma it seems possible that the cyst formation may allow for changes in pressure which could account for visual improvement. Also we have observed improvement in visual acuity when the patient harbored a meningioma. This individual during a first pregnancy was suspected of having a retrobulbar neuritis. During a second pregnancy there appeared involvement of both visual fields. Later she exhibited a bitemporal field defect and a suprasellar meningioma was removed at operation (page 1161 FBW, Case 416). In such a case it would seem that pregnancy activated the tumor.

Case 6

Hysteria, an erroneous diagnosis in a child who lost vision suddenly.

V. E. 106458 was seen through the courtesy of Dr. A. Kiel. She was a seven-year-old white girl. She had been out of school with what was said to be "flu" from January until the middle of February, 1952. She was in school early in April and complained to the teacher that she could not see. There had not been any earlier complaints as regards any defect in vision. Examination revealed nothing abnormal other than loss of vision.

At examination the pupils were dilated and fixed to light. There was no history of drops having been used. A drop of pilocarpine promptly resulted in narrowing of a pupil.

Because the discs were normal and there was total or near-total loss of vision the possibility of craniopharyngioma suggested itself. An air injection showed an abnormality of the third ventricle. Operation revealed a craniopharyngioma. The patient died.

Normalcy of roentgenograms in an individual with some loss of fields bitemporally characterized the case of R. P. 511188, a man, aged 57 years. We have come to feel that normal-appearing X-ray films are not strong evidence against tumors which are here considered. Mention has been made of the so-called Cushing syndrome—bitemporal field defects and optic atrophy with normal

or near-normal X-ray findings, signifying suprasellar tumor.

The case history which follows seems extremely important to me in regard to diabetes mellitus and optic atrophy. Briefly, it has never been agreed that optic atrophy may be dependent upon diabetes mellitus and it has not been generally accepted that diabetes mellitus may produce optic neuritis.

Stansbury has written a report on optic atrophy in diabetes mellitus; three individuals in one family were so affected. Wolfgram has reported on simple optic atrophy in several siblings all of whom suffered from diabetes mellitus. Tunbridge and Paley have written concerning optic atrophy in siblings. Their paper, which one of us (FBW) enjoyed reading before publication, should be consulted.

It becomes clear that optic atrophy occurring in young diabetics has been familial in several instances and the defects may or may not be related. Optic atrophy in a juvenile diabetic should suggest tumor unless other members of the family also exhibit optic atrophy and suffer from diabetes.

Through the courtesy of Dr. G. G. Gibson and Dr. W. E. Nelson, I have observed a 16-year-old girl (J. W. 8758-FBW) who developed diabetes at nine years of age. The diabetes was difficult to control. When she was 15 years of age, she developed defective vision and pronounced pallor of the temporal sides of the optic discs. There were paracentral scotomas above the point of fixation for each eye—X-ray examinations were not revealing. Dr. Gibson, Dr. Nelson, and I were agreed as regards the possibility of a craniopharyngioma but thought that, until there was further loss of vision from 20/30 and 30/50 and further changes in the fields, watchful waiting was in order.

Dr. Harriet Guild has told me that in looking after diabetic children in the Johns Hopkins Hospital for 25 years she has yet to see optic atrophy in such a child. Dr. Jonas Friedenwald did not think diabetes mellitus in itself causes optic atrophy. Thus, it would seem that optic atrophy in a child with diabetes mellitus is most unusual. We have such a case in which craniopharyngioma was found to be present at operation.

Case 7

History. A child, aged 18 months, was found to have diabetes mellitus. When the child was eight years of age, it was found that the visual acuity was defective, both eyes. X-ray films taken a year before examination at age eight years were said to be normal. There was bitemporal loss of visual field. X-ray abnormalities established the diagnosis of craniopharyngioma. Operation was undertaken.

M. H. (A66754) was diagnosed as suffering from diabetes mellitus at the age of 18 months. The diabetes was said to be relatively easily controlled.

A year before our examination in 1955, vision was said to have been 20/20 and 20/30 in the right and left eye respectively. Six weeks before we saw him there was loss of vision to 20/200 bilaterally.

At the time of our examination, vision was 3/70 for each eye. There was pronounced pallor of both optic discs. By confrontation there was loss of both temporal fields. X-ray films showed enlargement of the sella and there were calcium deposits above the sella.

After his diabetes was studied and controlled and while he was on cortisone, operation was performed (Dr. Chambers). The diagnosis of craniopharyngioma was verified; a large cyst was removed after evacuation of it. Three weeks after operation vision was 5-10/200 in the right eye and 20/70 in the left eye.

Pituitary tumors

In this study we reviewed 55 cases of pituitary tumor which have come to our attention. There were 46 chromophobe adenomas with 40 cases verified; seven were eosinophilic adenomas with one verified at operation. In addition, this group included one case of carcinoma of the pituitary (Dr. A. B. King); and a case diagnosed as teratoma affecting the chiasm (J. S. 593115).

Chromophobe adenomas. Only five cases were not verified by microscopic examination of tissue (C.W. 588032; A. D. 677848; J. R. 666700; R. O. 6506-FBW; W. T. 617993).

Four children suffered from chromophobe adenoma of the pituitary and in two instances presented features which are unusual with pituitary adenoma:

An 11-year-old girl was seen through the

courtesy of Dr. George Smith. Before operation, she exhibited a third-nerve paralysis. After operation, there was the development of a complete regeneration syndrome with misdirection of the affected third nerve. Elsewhere mention is made of frequent transient cranial nerve palsies with pituitary tumors, but misdirection of fibers in regeneration has been absent in other pituitary tumor cases we have observed.

The other child was a girl, eight years of age (D. H. 073541), seen through the courtesy of Dr. R. M. N. Crosby. This child was originally seen a year before I saw her because of failing vision in one eye. There was enlargement of the sella. At operation a chromophobe adenoma of the pituitary was removed. The visual acuity returned to approximately normal. A year later the visual acuity of one eye was perception of light and in the other 15/200. There was a recurrence of tumor proven at operation and subsequent autopsy (fig. 9).

Case 8

G. C., a boy, aged 14 years, was observed by Dr. Lloyd. In 1954 he fell from his bicycle and was unconscious for a short period. He was seen by a local physician and was not admitted to hospital. Ten months later he complained of defective vision. In one eye there was loss of light perception and a pale optic disc, and in the other eye vision was 20/20 with a normal disc. X-ray studies of the skull showed enlargement of the pituitary fossa. The field of the functioning eye was normal. Operation revealed a large chromophobe adenoma. The patient has done well.

Case 9

R. P. (670316), a boy, aged 16 years. Growth had been retarded for five or six years. Sexual development was defective. There was pronounced loss of temporal field of one eye and narrowing of the field of the other eye. Both discs were pale. X-ray studies revealed marked enlargement of the sella turcica.

Operation revealed a cystic chromophobe adenoma.

Twenty-seven patients were between 25 and 50 years of age. The oldest patient was 69 years of age (E. S. 705471). There were 26 females and 20 males. Twelve had a history of trouble for less than a year; 23 had trouble for two to five years; eight had symptoms for more than 10 years when the first examinations were made.

Pituitary dysfunction was present in 30 patients and, in some instances, more than one function of the pituitary was affected. Amenorrhea prior to the menopause was the most frequent single occurrence in 16 of 22

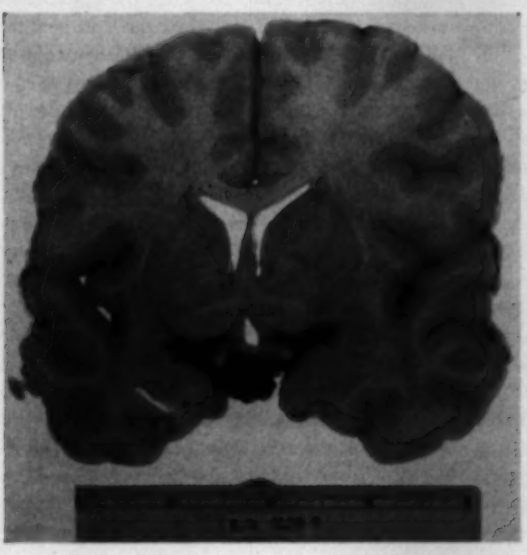


Fig. 9 (Walsh). Section through chromophobe adenoma of the hypophysis. (D. H. 073541.) (Courtesy of Dr. R. M. N. Crosby.)

female patients. Loss of libido was described in 10 of 18 males. Loss of secondary sex characteristics occurred in 12 individuals, acromegaly in three, diabetes insipidus in three, stunted growth in three. Although diabetes insipidus was rare preoperatively, it was a common occurrence after operation.

There were no complaints as regards vision in four individuals (E. A. 693248; S. C. 640558; A. D. 677848; E. N. 6229-FBW). E. A. and E. N. had bitemporal field defects. Homonymous hemianopsia was present in one (S. C. 640558). There was bilateral loss of vision in 10 patients and unilateral loss in 27 patients. Two patients had no light perception in an affected eye (E. L. 334150). Optic atrophy was bilateral in 19 and unilateral in 12. In one individual there was bilateral secondary optic atrophy associated with papilledema in the other eye (M. F. 460888).

Bitemporal field defects were present in 31 patients, homonymous field defects in three (H. R. 394249; C. W. 588032; J. P. 555233). Bilateral pericentral scotomas were found in only one individual (R. O. 6506-FBW) (case summary below). Unilateral central scotomas were found in four individuals (L. S. 356702; J. F. 455535; J. A. 267762; W. H. 401397).

As regards X-ray films of the skull, the sella turcica was enlarged in 29 patients; in 10 it was destroyed. Calcification above the sella suggested the possibility of craniopharyngioma in two patients (S. M. 449583; S. G. 274217). Eighteen patients received radiation therapy after operation and two in this group received radiation therapy prior to operation.

There was recurrence of tumor in from five to 19 years in five cases (R. C. 122135, 17 years; B. C. 227061, 12 years; E. L. 8961-FBW, four years; E. Z. 91653-Mercy, five years; N. F. 672930, 19 years). Three patients died shortly after operation.

Multiple diagnoses were made in two patients. In one, tabes dorsalis had been treated. The patient also suffered from a chromophobe adenoma (S. G. 274217). A brief abstract is offered subsequently. In another patient (A. T. 367925) an intracranial ligation of the carotid artery for aneurysm did not stop progressive failure of visual acuity which had been attributed to aneurysm; there was some destruction of the sella turcica. Two years after the operation for aneurysm a chromophobe adenoma of the pituitary was removed. She lost all useful vision.

Meningitis as a complication of pituitary tumor is rare. J. P. (555233) developed pneumococcal meningitis on her way to the hospital; she recovered on antibiotics and had a successful operative intervention. Staphylococcal meningitis occurred three years after operation for pituitary tumor in E. L. (334150). She made a good recovery. We have one other case of meningitis following removal of intracranial tumor (glioma of the optic nerve in C. G. (616646). Pneumococcal meningitis developed some three years after operation and produced death within 18 hours.

Unanticipated blindness developed after operation immediately or within a few days in two individuals. In one patient (G. P. 639106) before operation the vision had been hand movements and 20/30 in the right and left eyes respectively; after operation the patient was blind and had developed a right hemiparesis. In J. S. (151103) the preoperative vision was 20/20 and 4/200 in the right and left eyes respectively; after operation there was loss of vision including perception of light (according to the patient); 12 years later, vision was: R.E., no light perception; L.E., 5/200. Another patient, W. M., seen through the courtesy of Dr. John R. Simmons at Brooke Army Hospital, prior to operation had hand movements in the right eye and 12/400 in the left eye. Operation was uncomplicated and a chromophobe adenoma was removed. Although the optic discs appeared almost normal, there was no improvement in the visual acuity several weeks after operation.

Eosinophilic adenomas. Seven patients

were studied. The diagnosis was verified in only one case because most of these individuals were treated with X rays. There were five males and two females ranging from 27 to 42 years of age. All were acromegalic. One was a giant six feet, nine inches tall, weight 300 pounds (W. F. 497217). One patient had evidences of acromegaly for 30 years before our examinations were made (F. H. 516320); the others had evidences of acromegaly for one to seven years. Amenorrhea was present for eight years in a 32-year-old woman (H. S. 12778-FBW). Another had amenorrhea and hirsutism for two years (I. H. 683236). One had diabetes mellitus for two years (F. H. 516320). In J. B. (600208), there were complaints of paraesthesias of the wrists and hands for which operations for the "carpal tunnel syndrome" had been performed, without relief. Following radiation to the pituitary the symptoms disappeared.

The visual acuity was affected in three individuals all of whom had temporal field defects (F. H. 516320; G. M. 6341-CEI; I. H. 683226).

In only one of these seven patients was a surgical procedure undertaken. In an earlier report, surgical intervention was described in an individual who developed ophthalmoplegia and brief reference is made to this case below. Following radiation therapy, the visual acuity improved from 20/40 and 20/200 in the right and left eyes, respectively, to 20/40+2 and 20/100−1 (F. H. 516320).

Optic atrophy was visible with the ophthalmoscope in only one of three patients with acromegaly who had defective vision and field defects (G. M. 6341-CEI). That is two of three patients with acromegaly and some loss of vision and field defects had normal-appearing discs. Such an anomaly has already been mentioned as occurring with craniopharyngiomas where possibly the incidence of normal discs with loss of vision and fields is somewhat higher than with pituitary tumors—at least in our experience.

The sella was enlarged in all but one individual in this group.

Radiation therapy was utilized in all but one of the seven patients included in this study. In one individual (J. B. 600208) the condition worsened rapidly after radiation therapy.

Basophilic adenomas. Cushing's syndrome is characterized by a sudden onset of obesity localized to the trunk, face, and neck, and sparing the extremities; a plethoric appearance with purplish linea atrophica in the skin; sexual hypofunction with amenorrhea in females and impotence in males; hirsutism in females; weakness in the extremities and painful joints; hypertension and hyperglycemia.

It is unfortunate that such a clinical syndrome is more commonly associated with hyperfunction of the glucocorticoids of the adrenal cortex gland rather than a basophilic adenoma as Cushing originally described. We did not encounter such a case in the present series.

Résumé symptomatology pituitary tumors. As regards general symptomatology, pituitary dysfunctions are of prime importance. Sexual dysfunction is commonly present. Amenorrhea was present in 15 of 22 females who had chromophobe adenomas and in females who suffered from eosinophilic adenoma of the pituitary. Loss of libido was a feature in 10 of 18 males with chromophobe adenoma. In a giant who presumably suffers from eosinophil adenoma there is loss of libido. Other obvious evidences of hypopituitarism are wrinkled dry fine skin with loss of facial hair, loss of under-arm and pubic hair, and a general appearance suggesting hypothyroidism. Acromegalic features were present in three patients with chromophobe adenoma as well as the seven who were acromegalics.

Diabetes insipidus and diabetes mellitus are infrequent in cases of pituitary tumor; diabetes insipidus is a common occurrence with craniopharyngioma. Gain or loss of weight may occur. Headaches which have

been described as a common feature of pituitary tumor have not been a pronounced feature in our cases. Certainly we have been quite unable to recognize what has been described as a pituitary headache.

X-ray examinations of the skull in most instances of pituitary tumor show enlargement of the sella often with erosion which is likely to involve the floor. Often the posterior clinoids are eroded or they may be angulated; the anterior clinoids may be eroded. Calcium above the sella was present in three of our cases of chromophobe adenoma; such calcification suggests craniopharyngioma (which is often associated with enlargement of the sella since such tumors may extend through it). It is of extreme importance that the ophthalmologists see the X-ray films; living up to such a rule would have saved embarrassment in the case now cited.

Case 10

History. The patient, aged 55 years when first seen, exhibited bilateral optic atrophy with Argyll Robertson pupils.

Vision was: R.E., counts fingers; L.E., 20/100. Visual fields were concentrically contracted, with ill-defined central defects. The patient was given penicillin and malaria therapy on the basis of serologic tests and threat to vision. Visual acuity remained at the same levels for seven years, then suddenly failed. X-ray films revealed an enlarged sella. At operation, a chromophobe adenoma was removed, with recovery of vision to previous levels in the better eye. Earlier roentgenograms had been reported as normal.

S. G. 274217 was thought to exhibit optic atrophy as a result of tabes dorsalis. Physical examinations supported the diagnosis as did serologic tests. A routine X-ray examination of the skull was made and it was reported as normal. When the patient was presented with sudden loss of vision in his one useful eye, another X-ray film of the skull was made (elsewhere). It showed pronounced and unmistakable enlargement of the sella. Operation for pituitary tumor resulted in a return of his vision to former levels.

Comment. Undoubtedly if the syphilologist or ophthalmologist (FBW) had looked at the original X-ray films, delay in diagnosis would not have occurred in this patient.

Ocular symptomatology pituitary tumors. Five individuals among 45 with chromophobe adenoma of the pituitary had no complaints as regards visual loss. Two individuals had normal vision and normal fields. Two had bitemporal field defects and of these there was pallor of one optic disc in one patient. One had homonymous defects in the visual fields. With the single exception mentioned the optic discs appeared normal in these five patients.

Of the seven eosinophilic adenomas, five patients had normal optic discs, normal vision, and normal fields. Loss of vision was bilateral in 11 cases of chromophobe adenomas and in two individuals with eosinophilic adenomas. Unilateral loss of vision was present in 27 individuals with chromophobe adenoma and in one with eosinophilic tumor. In two patients there was total blindness in one eye with chromophobe adenoma (E. L. 334150). It is interesting that suprasellar tumors, as for example meningiomas, account for total loss of vision in one eye oftener than intrasellar tumors.

Field defects were usually bitemporal. Such defects were present in 29 patients with chromophobe adenoma and in two patients with eosinophilic adenoma. As regards bitemporal field defects, such defects invariably signify involvement of the chiasm. Whether the entire temporal half-fields are affected or only small paracentral scotomas are present makes no difference as regards localizing significance. This is shown in Figure 10, in the field of the right eye, where an absolute scotoma is shown and in the field of the left eye where there is loss of the temporal field for red, as well as loss of peripheral field to a large white object.

As regards the mechanisms responsible for field defects in pituitary tumor, a paper by Rucker and Kernohan is important. They suggested that the upper bitemporal hemianopsia which occurs so commonly with pituitary tumors may be due to interference with the blood supply of the anterior margin of the chiasm through pressure. Similarly, defects in the lower portion of the visual fields may be due to forcing of the tumor against the anterior cerebral and anterior communicating arteries.

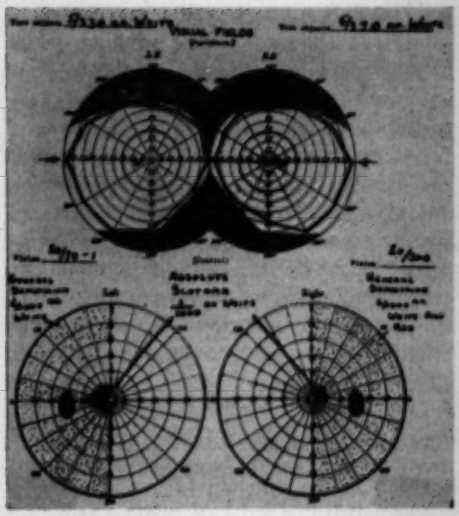


Fig. 10 (Walsh). Bitemporal field defects in a case of pituitary tumor (W. H., chromophobe adenoma.)

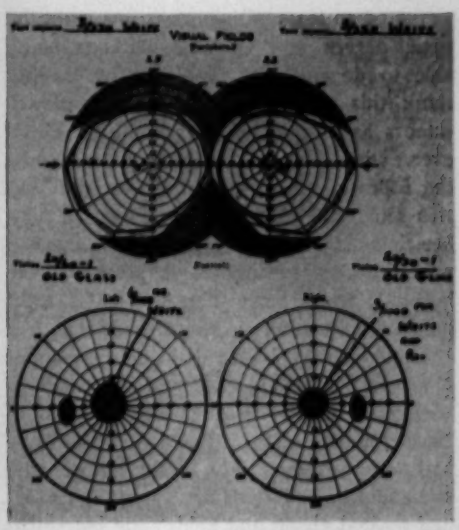


Fig. 11 (Walsh). Central defects in a case of pituitary tumor. (Preoperative, R. O'M.)

Central defects in the visual fields were found in five patients. In two they were bilateral (R. O'M. 6505 (FBW); J. A. 267762). In R. O'M. (fig. 11) the field defects were relatively circular pericentral scotomas as shown below. In J. A., the visual acuity of one eye was so low that one could not be sure regarding fixation.

Unilateral central field defects were present in three patients (L. S. 356702; W. H. 401397; J. F. 455535). Excepting in one of these patients (L. S., fig. 12), there was involvement of the temporal field of the opposite eye.

We routinely use colored test objects in testing the fields of individuals suspected of having a chiasmal involvement. It is our belief that in such cases use of a six mm. or even 10 to 12 mm. red object at a meter will show up a loss of temporal field rapidly when one may not be satisfied with using small white objects. I cannot refrain from stating in passing that our patients are entirely unreliable when it comes to using small white test objects at a meter (one and two mm.)

Homonymous field defects were present in three patients with chromophobe adenomas (H. R. 394249; C. W. 588032; J. P. 555233).

Changeability of visual fields has in some instances made it difficult to evaluate the

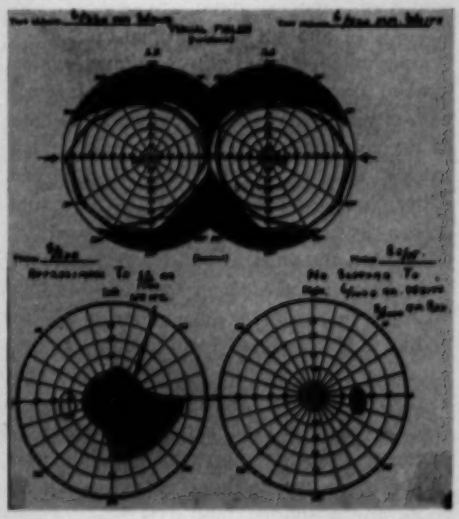


Fig. 12 (Walsh). Unilateral field defect in a case of pituitary tumor. (L. S. 356702.)

status of patients with tumors involving the optic nerves and chiasm. Without being able to document it, I personally do not think this occurs as often with pituitary tumors as with craniopharyngiomas. However, with proven chromophobe adenoma the following case is cited. J. P. (555233) was sent for examination and carried with her fields showing bitemporal loss; she had pneumococcus meningitis on arrival at the hospital; when I saw her, she had a right homonymous defect in the visual fields.

Optic atrophy visible with the ophthalmoscope is the rule in cases of chromophobe adenoma. In our series it was bilateral in 20 and unilateral in 12 patients. We have had seven patients with chromophobe adenoma and normal optic discs; one individual had normal vision and fields; one individual had normal vision but bitemporal field defects; four patients had defective vision, defective fields, and normal optic discs. There was one case of bilateral secondary optic atrophy seemingly dependent upon a previous papilledema. There was one unilateral papilledema associated with optic atrophy in the other eye (M. F. 460888). In the eosinophilic group there was one example of bilateral optic atrophy (G. M. 6341-CEI) and six with normal discs.

Ophthalmoplegia with pituitary tumor. Cranial nerve palsies occur in association with pituitary tumor much oftener than most of us have realized. The frequency of such palsies was made clear by Weinberger, Adler, and Grant who pointed out that such palsies were the result of involvement of the cavernous sinus.

In 1949, I reported on two cases of total bilateral ophthalmoplegia occurring in individuals who suffered from pituitary tumor. In these two cases it seemed obvious that the symptomatology as regards the eyes was not the result of the extrasellar extension of tumor as has been described by Jefferson.

There are two mechanisms that could account for a sudden total external ophthalmoplegia: (1) Hemorrhage into the tumor and possibly into the adjacent cavernous sinus, (2) sudden extreme swelling of the tumor with direct pressure on the adjacent cavernous sinus of one or both sides as occurred in the two cases mentioned above.

Jefferson's and my paper contain diagrams and drawings which clarify the anatomy of the situation. In this series mention has already been made of a case of third-nerve palsy present before operation with the regeneration syndrome developing after operation (J. S.—courtesy of Dr. George Smith).

Case 11

At this time we have under observation an interesting woman patient, aged 50 years, who undoubtedly harbors a pituitary tumor (E. H. 14397). Her only complaint has been diplopia. There is a right sixth-nerve palsy, present for six months. This has become gradually more severe. The vision, visual fields, and optic fundi are normal. X-ray films reveal pronounced increase in the size of the sella turcica. She is currently receiving a course of X-ray treatments.

This case is of particular interest from the standpoint of indications for operation. It is our feeling at this time that gradually developing ophthalmoplegia alone is insufficient reason for operative intervention.

Treatment. It is not our purpose to consider therapy here. It has been the practice in The Johns Hopkins Hospital to treat eosinophilic adenomas with radiation therapy and, in most instances, to operate upon chromophobe adenomas. In those instances in which the visual acuity and the visual fields remain normal it has been our belief that operative interference is contraindicated.

Malignant nasopharyngeal tumors

We have studied 10 cases of proven malignant nasopharyngeal tumor. The symptomatology of such tumors is: pain in the face or in or about the eye; episodes of interference with hearing (involvement eustachian tube); cranial nerve palsies which are usually unilateral and multiple; invasion of the brain with involvement of chiasm; in-

vasion of the orbit with exophthalmos; infiltration of the palate; cervical lymphadenopathy which tends to be bilateral.

These tumors extend from the fossa of Rosenmüller or from the paranasal sinuses along the dura. They are at first extradural but grow through the various foramina at the base. Some such tumors are essentially epithelial, whereas, others are sarcomas. Radiation gives temporary relief in many instances. According to Godtfredsen cures may be anticipated in a fair number but we have seen no successes.

Particular mention is made here of what we consider the outstanding symptom suggesting nasopharyngeal tumor. There is involvement of the fifth nerve in a majority of cases. In our present series eight patients had pain which developed spontaneously. In seven of eight cases, it was present in the region of the second division of the fifth nerve. One of us has suggested that the anatomic arrangement about the eustachian tube makes the second division particularly vulnerable.

Certainly next in importance is the development of multiple cranial nerve palsies which are unilateral. Godtfredsen has emphasized the importance of such nerve palsies. He has said that if one finds a paralysis of the 12th nerve associated with paralysis of the nerves supplying the ocular muscles certainly the patient has a nasopharyngeal tumor. New of the Mayo Clinic made us aware of this tumor in this country.

Anyone experienced with nasopharyngeal tumors knows the frequency with which the diagnosis is missed. In all cases where such a tumor is suspected there should be a careful examination of the nasopharynx and it is obligatory that a nasopharyngoscope be used. A biopsy should be taken from the fossa of Rosenmüller. A single biopsy may be negative. The mucous membrane in the fossa of Rosenmüller. A single biopsy may underneath it there may be a flat tumor. The next case summary illustrates a temporary misdiagnosis in such a case.

Case 12

F. G. (523253), a 62-year-old white woman, complained of defective vision in the right eye. The eye was proptosed four mm. and it was immovable. There was complaint of pain principally in the region of the second division of the fifth nerve. It was suspected that a malignant nasopharyngeal tumor was present.

An examination of the throat was declared to give normal findings and the fossa of Rosenmüller seemed normal. Corneal sensation seemed normal. An arteriogram was read as normal.

A craniotomy was performed and the orbit was unroofed. An epithelial tumor was found in the depths of the orbit. A belated biopsy from the fossa of Rosenmüller revealed carcinoma (Schminke's tumor). A year later there was pronounced optic atrophy. In a further year the patient died.

Here we are not going to go extensively into the problems concerning differential diagnosis of malignant nasopharyngeal tumors. However, attention is drawn to the similarity between the symptoms which result from malignant parotid gland tumors and nasopharyngeal tumors as described by Dr. A. B. King. Also chordomas produce similar symptomatology.

We have observed a patient with metastatic carcinoma to the gasserian ganglion from the breast. She exhibited a left abducens palsy, left corneal anesthesia, and proptosis of the left eye to the extent of three mm. She had complained of pain in the left face for 10 months and diplopia for 13 weeks. Dr. James Watts severed the posterior root of the fifth nerve and established the diagnosis (F. H. 7618-FBW).

Hypophysectomy for metastic tumors. Although really far afield from neuro-ophthalmology, we have included a short section of hypophysectomy for metastatic tumors on the basis of its great interest only. Dr. W. W. Scott, with Dr. A. E. Walker, has been responsible for the major part of the work done in The Johns Hopkins Hospital and we have details on five cases. Olivecrona described a larger series: 26 patients, including three with Cushing's syndrome, seven with malignant hypertension, four with diabetes, and 12 others with malignant tumors.

The basis for this procedure is roughly as follows. Prior to sexual maturation, hypophysectomy will prevent the development of secondary sexual characteristics. After puberty, hypophysectomy results in involution of sexual organs, including an appreciable shrinkage of the prostate gland. The hormones responsible probably consist of luteotrophin as well as gonadotrophin.

Experimentally it has been shown by Evans that neoplasms of the adrenals can be produced in rats by injecting pituitary growth hormones. Such neoplasms can be prevented by hypophysectomy in the rats, and also hypophysectomy makes it impossible to produce tumors by the injection of methylcholanthrene.

Dr. A. E. Walker performed six cases of hypophysectomy for treatment of malignant tumors which had not responded to radiation or hormone therapy. Both Olivecrona and Walker stressed the extreme difficulty in attempting removal of the entire pituitary. Of the cases in which Walker operated, all six with carinoma of the prostate died within a little more than a year. Olivecrona operated on three patients for diabetes mellitus and one was successful. Death in six of 10 patients (three for diabetes mellitus and seven for malignant hypertension) was the result of cerebral edema.

At this time there would seem to be some justification for doing this operation in cases of metastatic carcinoma of the breast and of the prostate, also chorionic epitheliomas not controlled by radiation or hormonal therapy.

Optochiasmic arachnoiditis

This entity is mentioned briefly because the affection can mimic tumor closely. Furthermore, along with other colleagues in The Johns Hopkins Hospital, one of us (FBW) until recently has not been entirely satisfied that such a localized affection really existed. In some instances, it results in symptoms and signs essentially those regularly associated with pituitary tumors. Here only two case records are summarized:

Case 13

History. A 47-year-old physician complained of decreased visual acuity in the left eye in June, 1952. In October, 1952, vision in the right eye became defective. Visual fields suggested chiasmal involvement. In 1953 operation revealed optochiasmic arachnoiditis. Recovery.

W. W. E. (10669-FBW) with correction had 20/40— and 20/50— vision in the right and left eyes, respectively. There was questionable pallor of the temporal side of the right disc and definite pallor of the left optic disc. The fields suggested chiasmal involvement.

In March, 1953, Dr. Frank Otenasek operated. There was improvement in the visual acuity within a week after operation and, after several months, vision of the right eye was 20/15 and of the left eye, 20/15. A paracentral scotoma could still be found in the central field of the left eye; the scotoma in the right visual field had cleared (fig.13).

Case 14

History. A 43-year-old man had blurred vision both eyes for nine months. Vision was: R.E., 20/200; L.E., 20/70—1. Fields suggested chiasmal involvement. Craniotomy was performed. There was no evidence of tumor but adhesions surrounded the chiasm and optic nerves (which were remarkably short). Ten months later visual acuity was normal in both eyes.

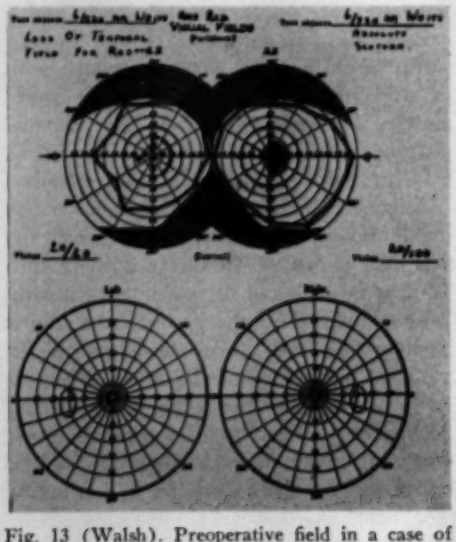


Fig. 13 (Walsh). Preoperative field in a case of optochiasmic arachnoiditis (W. E.)

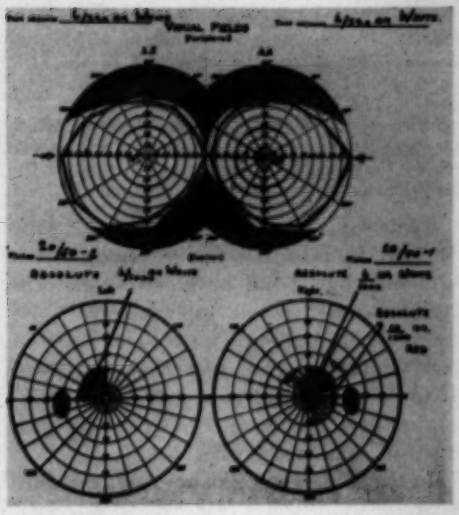


Fig. 14 (Walsh). Preoperative field in a case of arachnoiditis.

J. S. (11569-FBW), who had been deaf most of his life, developed defective vision in both eyes. All examinations other than of the eyes gave normal findings. Craniotomy revealed adhesions about the optic nerves and chiasm. A week after operation visual improvement was noted. Within a few weeks vision was: R.E., 20/60; L.E., 20/40. Ten months after operation visual acuity was 20/20 for each eye (fig. 14). (Courtesy of Dr. John Chambers.)

Third ventricle tumors

Colloid cyst of the third ventricle is a primary tumor. Solid tumors originate in the roof of the ventricle. Particularly with cystic tumors there is likely to be a ball-valve action of the tumor within the ventricle. Headaches are incited by bending, straining, or stooping. As time progresses, the clinical picture changes. With the headaches, there is a slow feeble pulse and a fall in blood pressure. Spells of unconsciousness may become a feature (see Ford). Doubtless the symptoms in addition to headaches represent pressure on or invasion of the hypothalamus. Papilledema tends to occur late; it is the most frequent single ocular sign. Signs of pituitary dysfunction are not present in these cases.

Our material contains five cases of third ventricle tumor (N. A. 698664; W. B. A37570; J. A. 453305; J. C. 690610; D. T. 435682). In three cases there was increased intracranial pressure. In three there was enlargement of the sella with erosion. Papilledema was present in two; bilateral optic atrophy in two; normal discs in one. One patient exhibited an homonymous hemianopsia; two had bitemporal field defects.

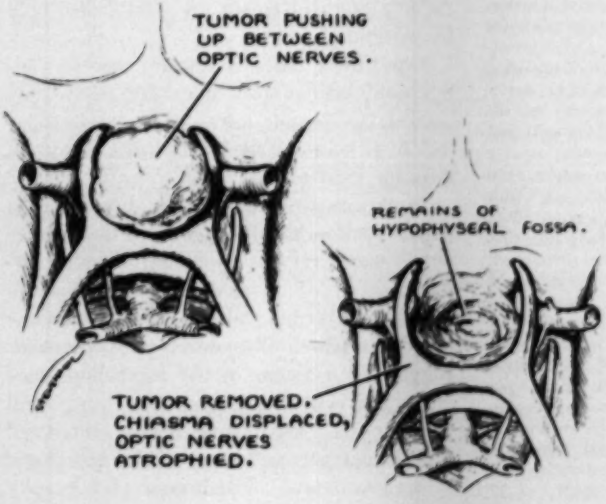

TUMOR PUSHING UP BETWEEN OPTIC NERVES.
REMAINS OF HYPOPHYSEAL FOSSA.
TUMOR REMOVED. CHIASMA DISPLACED, OPTIC NERVES ATROPHIED.

Fig. 15 (Walsh). An unusual ependymoma. (Courtesy of Dr. Frank Otenasek.)

There was no example of binasal hemianopsia. There was a sixth-nerve paralysis in one case.

Misdiagnosis of pituitary tumors when posterior fossa tumor is present

From time to time pituitary tumor is diagnosed when actually a posterior fossa tumor is present. Such an error can occur for a variety of reasons, some of which are now set forth in brief case reports.

Case 15

History. Glioma of the left cerebellum was found at operation when preliminary diagnosis was pituitary tumor on the basis of bitemporal visual field defects. There was elevated spinal fluid pgotein. Ventriculograms, showing dilated lateral and third ventricles, pointed to the site of trouble.

A. N. (698623), a 73-year-old white woman, complained of defective vision for two months. Dizziness present for four months. The conjugate deviation of the eyes to the left was slightly defective. Simple optic atrophy left optic disc and pallor right disc were present. There were medullated nerve fibers of left optic disc. Skull X-ray films were normal. Neurosurgeons explored the posterior fossa and found a glioma of the left cerebellar hemisphere. (Courtesy of Dr. Frank Otenasek.)

Case 16

History. A 46-year-old man had headaches for six months. There was questionable left homonymous hemianopsia. Hyperesthesia was present over the first division left fifth nerve, first division. Air studies showed a tumor to be in the posterior fossa.

M. E. C. (1760-FBW) had symptoms suggesting cerebral degeneration and it was thought for a time that he had frontal lobe involvement. Air injection directed the neurosurgeons to his posterior fossa. A benign tumor was removed.

At the time I saw the patient, two weeks after operation, there was a history of loss of vision both eyes. Acuity was: R.E., questionable light perception; L.E., 2/50 few letters. There was pronounced bilateral optic atrophy.

Case 17

History. A 44-year-old woman had a meningioma of the posterior fossa misdiagnosed as pituitary tumor because of enlargement of the sella.

A. A. (362823) complained of headaches and unsteadiness for seven years, with poor vision for a few months. There was occasional horizontal nystagmus to the right. Right corneal reflex was diminished. Vision was: R.E., 20/20; L.E., 20/30-4. Visual fields were normal. There was low-grade papilledema, more marked on the left. There was weakness of muscles innervated by the fifth nerve (first and second divisions), ninth, tenth, twelfth. The right sella turcica was enlarged. The ventricles were dilated and a mass appeared below the right lateral ventricle. At operation a mass extended from the right posterior fossa through the tentorium into the superior temporal region.

Comment. It becomes clear that the cardinal features of pituitary tumor, visual loss with bitemporal field defects and enlargement of the sella turcica, may be associated with posterior fossa tumors as also may peripheral ocular cranial nerve palsies. It would seem from these cases that air injection only can serve to differentiate such cases in some instances.

In the section on colloid cysts of the third ventricle we include a case (W. B. A37570), a four and one-half year-old white boy who had vomiting, bilateral papilledema, and a right sixth-nerve palsy with separation of the sutures. Visual acuity was normal for both eyes. No field defects were found. On the basis of probabilities a diagnosis was made of cerebellar tumor. Air studies revealed the site of involvement and subsequent operation verified the presence of a third-ventricle cyst. A year after operation vision was normal for both eyes. Both discs appeared slightly pale. In all four cases cited the site of involvement was established only by injection of air.

From these cases it appears that (1) bitemporal hemianopsia does not necessarily indicate an organic intrasellar or suprasellar lesion. (2) an enlarged sella turcica may not indicate local tumor.

In this regard attention is directed to a paper by Zondek. He described a 52-year-old woman who was obese and had alternating periods of insulin-insensitive diabetes and hypoglycemia; also a highly unstable blood pressure. She developed symptoms suggesting a lesion in the cerebellopontine angle and, with these symptoms, bitemporal hemianopsia. Dehydrative therapy eliminated the hemianopsia and most of the neurologic symptomatology. Pneumoencephalography

and electroencephalography were both negative. The author stated he had observed eight cases in which disturbances of water and salt metabolism gave origin to bitemporal hemianopsia.

Remarkable and unusual cases

Ectopic pinealoma

Ectopic pinealoma involving the chiasm gives symptoms and signs which are indistinguishable from pituitary tumor in some cases. Our single case of such a tumor offered problems in diagnosis. Ultimately visual acuity was totally lost in both eyes.

Case 18

History. A 17-year-old white boy had blurred vision for nine months. There was a history of headaches, polyuria, thirst for four years, and a story of transient weakness of the legs two years before examination. The optic discs appeared normal. Visual fields are shown in Figure 16. X-ray studies were negative. The tumor was thought to be craniopharyngioma after the first operation. The diagnosis of ectopic pinealoma was made at the second operation.

R. G. (560741) gave a not-too-convincing history of thirst, headaches, and polyuria for four years and transient weakness of legs. A trabeculated cyst was present at the site of an old left-arm fracture and this, with the alleged diabetes insipidus, suggested Schüller-Christian disease. X-ray films were negative. Vision was: R.E., 20/40—2; L.E., 20/400. The optic discs appeared quite normal. Visual fields are shown in Figure 16. At this time the possibilities seemed to be (1) disseminated sclerosis, (2) Schüller-Christian disease, (3) tumor.

Craniotomy revealed what was thought to be a craniopharyngioma. After operation, the vision was: R.E., 20/20 with a temporal field loss, and L.E., light perception. Four months later vision was: R.E., 20/100; and L.E., quite blind. Reoperation was performed. Following this there was complete blindness. The optic discs remained normal. The tumor was described as ectopic pinealoma. Heavy radiation was given. The patient remained entirely blind. The optic discs were extremely white within one year after the operation (first operation).

Pearly body tumors (epidermoid tumors)

These tumors originate from the meninges or from the choroid plexus and rather often develop in the interpeduncular cistern, where

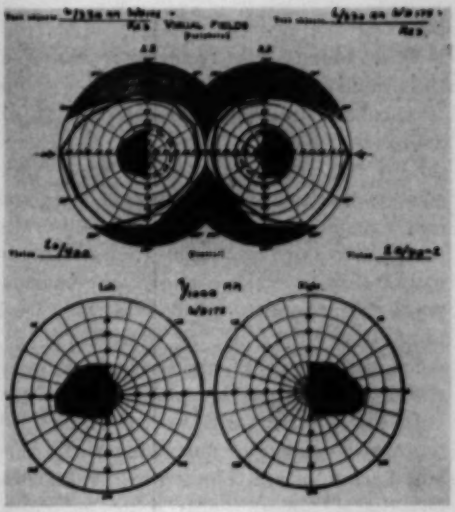


Fig. 16 (Walsh). Preoperative field in a case of ectopic pinealoma. (R. G. 560741.)

they may cause pressure on the chiasm and extend upward into the third ventricle (Ford). We have had such a case, now briefly summarized.

Case 19

History. A 25-year-old white man had gradual decrease in visual acuity for three years, with diplopia for two years. Vision was R.E., 15/200; L.E., 20/200. There were bitemporal field defects and bilateral optic atrophy. Partial removal of a midline pearly-body tumor was accomplished. Extensive progress of the tumor was reason for reoperation six years later.

R. C. (270506) on his first admission was found to have a midline pearly-body tumor extending from the interpeduncular cistern forward to the tip of the frontal fossa and into the temporal lobe and sylvian fissure into the posterior fossa. As much of the tumor as possible was removed. Following operation vision was improved to: R.E., 20/200; L.E., 20/50.

Six years after the first operation was performed the patient returned with convulsions and dizziness. More of the tumor was removed. It had become bilateral and filled the floor of the middle fossa.

Thirteen years after the operation a third operation was performed. There was complaint of dizzy spells and lethargy. The right eye was completely blind. The vision of the left eye was 20/20 in a small lower nasal quadrant of field taking in the point of fixation.

Skull X-ray films, excepting for defects produced by operations, remained quite normal.

Chordomas

These tumors arise from the remnants of the primitive notochord found on the clivus Blumenbach in about two percent of all autopsies (Ford). They originate extradurally but often penetrate the dura. They arise in the base of the sphenoid bone and may extend into the nasopharynx or orbits or into the third ventricle. They are likely to press on the chiasm and produce bitemporal hemianopsia. X-ray studies reveal some destruction of the sphenoid bone. Adenocarcinomas of the hypophysis give rise to similar symptomatology (Ford).

In this present study we have examined the records of two of our patients who harbored chordomas. Chordomas and nasopharyngeal tumors (also some malignant parotid gland tumors—King) produce multiple unilateral cranial-nerve palsies.

Case 20

History. P. W. (668183), a 67-year-old white woman, gave a history of ptosis of the left upper eyelid 17 years before examination. The ptosis persisted for one month. It recurred six years before examination and persisted. There was a history of several convulsions during six years. There was complaint of a sensation of a mass in the throat present for two years. There was paresis of the third and fourth nerves, second and third division of fifth, sixth, and eighth on the left. X-ray studies of the skull revealed a soft tissue mass at the base.

There was a history that chordoma had been removed from the region of the left temple several years earlier. The patient decided to have neither surgical nor deep X-ray therapy at the time.

In another case (W. G. 350597), chordoma did not exemplify multiple nerve palsies.

Gowers, Paton, Foster-Kennedy syndrome

I am hesitant to state that, in this considerable number of cases of tumor, I can cite only one case which I consider to exemplify this particular syndrome (E. T. 701671). A 57-year-old woman showed optic atrophy on the right and papilledema on the left. I did not show a central scotoma in the field of the atrophic eye because of lack of co-operation on the part of the patient.

Glioblastoma of left frontal lobe with internuclear palsy

Certainly in most instances an internuclear palsy indicates a lesion within the brain stem, consequently an inoperable lesion for the neurosurgeon. We have observed an individual who suffered from a hemispheric glioblastoma multiforme and yet exhibited an internuclear palsy.

Case 21

History. Anterior internuclear palsy, a false localizing sign in a case of hemispheric tumor. This case is of unusual importance.

G. F. (559857), a 34-year-old man when first seen, complained of severe headache for a period of eight weeks during which time he had been euphoric. Clinical examination revealed a left anterior internuclear palsy and low-grade left-sided papilledema. Arteriograms and air injection supported the idea of there being a left-sided hemispheric involvement but exploration failed to reveal tumor.

Three months after operation the patient died. Autopsy revealed a glioma extending from the left frontal lobe to the corpus callosum and within the meninges. There was no tumor in the brain stem.

Comment. I believe that this case summary indicates the only occasion on which I have seen an anterior internuclear paralysis which seemed to be a false localizing sign. From time to time in individuals with increased intracranial pressure a palsy of conjugate movement may not indicate involvement of the brain stem when this localization would seem reasonable but palsies of conjugate movement may originate in hemispheric lesions. Not so internuclear palsies which almost invariably indicate an intrinsic lesion within the brain stem.

Case 22

History. Enlarged optic foramina in bilateral oligodendroglioma of the frontal lobes. Right optic canal enlarged. Right papilledema. Right blindspot enlarged. Diplopia. Large bifrontal tumor found at operation. Postoperative weakness seventh, ninth, eleventh, and twelfth nerves.

E. H. (394885), a 29-year-old white man, complained of diplopia and headaches for five months and weakness left arm and leg for six weeks prior to first examination. Vision was 20/30—1 in the right eye and 20/20 in the left eye. There was a right papilledema of four diopters without protrusion of the eye; the left optic disc was normal. The optic foramen on the right was markedly enlarged.

At operation it was shown that there was an inoperable glioblastoma involving both frontal lobes.

Case 23

History. Cerebral tumor in individual suffering from retinitis pigmentosa.

R. W. (650030), a 48-year-old white man, had had a severe auto accident 26 years before examination. The right eye was always weaker than the left after the accident. He had had headaches for four weeks prior to examination.

Vision was: R.E., with correction, 20/30; L.E., 20/20. There was bilateral papilledema in a fundus which had a classical appearance of retinitis pigmentosa. There was a ring scotoma in the visual field of each eye.

At operation a meningioma was removed from the region of the left parietal lobe.

Case 24

History. E. W. (709603). Glioblastoma involving the right lateral ventricle and extending into the third ventricle to involve the chiasm accounted for papilledema with optic atrophy, bilaterally. Visual fields were narrowed to two- to three-degree circles. Visual acuity remained at 20/20 and 20/50—2 in the right and left eye, respectively.

Retinoblastoma

In this communication no mention is made of retinoblastoma up to this point. The diagnosis of retinoblastoma usually is made while the tumor is intraocular. In some instances, at the time of enucleation of an eye, it is found that the tumor has extended along the nerve to involve the brain. Actually the optic nervehead may be invaded by retinoblastoma.

When the nervehead has been invaded, there may be involvement of the stem of the nerve to about the level of the central retinal vessels. The tumor cells then extend along the spaces about the nerve and brain where they produce a so-called tumor meningitis.

In this paper mention is made of only one point as regards intracranial involvement with retinoblastoma. That point concerns removal of the intracranial optic nerve, and is dependent upon the anatomy of the nerve. It is vital not to sever the nerve close to the chiasm because, by so doing, a loss of temporal field is initiated in the otherwise sound eye. I have seen this untimely incident occur only once.

Case 25

History. A 33-year-old white woman had loss of vision in the left eye for one year and a gradual decrease of vision in the right eye for a few weeks. Menses were irregular for one year. Vision was: R.E., 20/20; L.E., hand movements. There were bitemporal field defects and optic atrophy, left eye. Surgical removal of an intraneural cyst from the left optic nerve and chiasm was done. Recovery was satisfactory.

E. D. (712434) had dull temporal headaches, irregular menses, and poor vision in the left eye for one year. She had been taking thyroid for a low basal metabolic rate. The vision began to fail in the right eye a few weeks before admission. Examination of the eyes showed nothing remarkable externally. There was pronounced pallor of the left optic disc. There was an extensive defect in the right visual field. Both maculas appeared "moth eaten."

Neurologic examination gave normal findings excepting as regards the eyes.

X-ray films of the skull were normal and a right carotid arteriogram was reported as negative.

At operation the left optic nerve was yellow and flattened. A bluish cyst seemed to be within the left optic nerve as shown in Figure 17. The cyst extended into the chiasm and region of the third ventricle. About 20 cc. of oily xanthochromic fluid

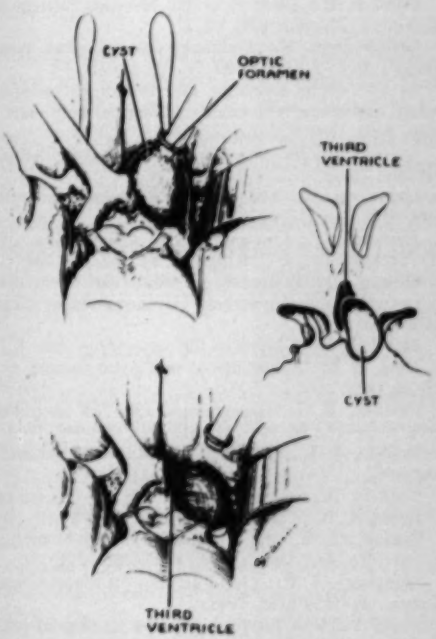


Fig. 17 (Walsh). Drawing of a cyst of the optic nerve. (E. D. 712434.)

was removed from the cyst. The cyst wall was cut through about two cm. posterior to the optic foramen.

After operation, the vision remained at 20/20 for the right eye. The temporal field defect persisted. The patient returned to her work as a school teacher.

Comment. Dr. Lorenz Zimmerman has studied the section. He has stated that the cyst is lined by stratified squamous epithelium. There is softening and pronounced astrocytosis about the cyst. Dr. Zimmerman has pointed out that epithelial cysts in the region of the third nerve may or may not be associated with craniopharyngioma. When not associated with craniopharyngioma, they are more typically epidermoid than in this case. Undoubtedly the tumor was a craniopharyngioma.

Conclusion

This paper is based on studies of 169 (153 verified) cases of tumors affecting the anterior visual pathways. Unusual features are stressed in this paper for the most part by case records. The paper does not lend itself to summarizing.

14 West Mount Vernon Place (1).

References

Cordes, F. C., and Hogan, M. J.: Primary malignant melanoma of the optic disc. Tr. Am. Ophth. Soc., **46**:201-217, 1938.

Coston, T. O.: Primary tumor of the optic nerve: With report of a case. Arch. Ophth. **15**:696-702, 1936.

Cushing, H.: The basophilic adenoma of the pituitary body and their clinical manifestations (pituitary basophilism). Bull. Johns Hopkins Hosp., **50**:137-195, 1932.

Davis, F. A.: Primary tumors of the optic nerve: A phenomenon of Recklinghausen's disease. Arch. Ophth., **23**:735-821; 957-1022, 1940.

Fincher, E. F.: Experiences with meningiomas. Surg. Clinics North Am., 1954, **34**:1037-1049, 1954.

Fischer, F.: Schwangerschaftsveranderung der Hypophyse abs Ursache Bitemperaler Hemianopsie. Ztschr. f. Augenh., **75**:343-354, 1931.

———: Ueber die Ursachen bitemporaler Hemianopsie bei Schwangerschaft. Ztschr. f. Augenh., **85**: 88-108, 1935.

Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence. Springfield, Ill., Charles C Thomas, 1952, ed. 3.

Godtfredsen, E.: Ophthalmo-neurological symptoms in connection with malignant nasopharyngeal tumors. Brit. J. Ophth., **31**:78-100, 1947.

———: Ophthalmologic and neurologic symptoms of malignant nasopharyngeal tumors: A clinical study comprising 454 cases with special reference to histopathology and the possibility of earlier recognition. Acta. Ophth., Supp. 22, 1944.

———: Studies on orbital tumors; exophthalmos due to malignant tumors in paranasal sinuses. Acta. Ophth., **25**:295-310, 1947.

Hagedorn, A.: The chiasmal syndrome and retrobulbar neuritis in pregnancy. Am. J. Ophth., **20**:690-699, 1937.

Jefferson, G.: On compression and invasion of the optic nerves and chiasm by neighboring gliomas. Tr. Ophth. Soc. of U. Kingdom, **65**:262-304, 1945.

King, A. B.: Traumatic encephaloceles of the orbit. Arch. Ophth., **46**:49-56, 1951.

Luft, R., and Olivecrona, H.: Experiences with hypophysectomy in man. J. Neurosurg., 1953, **10**:301-316, 1953.

Marshall, D.: Glioma of the optic nerve. Am. J. Ophth., **37**:15-36, 1954.

New, G. B.: Syndrome of malignant tumors of the nasopharynx: A report of 79 cases. J.A.M.A., **79**: 10-14, 1922.

Pfeiffer, R. L.: Roentgenography of exophthalmos with notes on roentgen ray in ophthalmology. Am. J. Ophth., **26**:724-741; 816-833; 928-942, 1943.

Poppen, J. L., and King, A. B.: Chordomas: Experience with thirteen cases. J. Neurosurg., **9**:139-163, 1952.

Penfield, W., and Hortega, del Rio, P.: Quoted from Reese.

Reese, A. B.: Tumors of the Eye. New York, Hoeber, Inc., 1953, ed. 1, pp. 144-168.

Rucker, C. W., and Kernohan, J. W.: Notching of the optic chiasm by overlying arteries in pituitary tumors. Tr. Am. Ophth. Soc., **51**:77-92, 1953.

Stansbury, J. R.: Optic atrophy in diabetes mellitus: A report of three cases in one family. Am. J. Ophth., **31**:1153-1163, 1948.

Scott, W. W.: Role of pituitary in normal and abnormal prostatic growth. Tr. Am. A. Genito-Urin. Surgeons, **46**:33-39, 1954.

Silver, L., and Henningar, G.: Cerebellar hemangioma (hemangioblastoma): A clinicopathological review of 40 cases. J. Neurosurg., **9**:484-494, 1952.

Taveras, J. M., Wood, E. H., and Mount, L. A.: Value of radiation therapy in management of glioma of the optic nerves and chiasm. Arch. Neurol. & Psychiat., **73**:702-703, 1955.

Walsh, F. B.: Bilateral total ophthalmoplegia with adenoma of the pituitary gland. Arch. Ophth., **42**: 646-654, 1949.

———: The ophthalmo-neurologic signs of malignant nasopharyngeal tumors. Canad. Ophth. Soc., **1**: 81-102, 1948.

Walsh, F. B., and Dandy, W. E.: Pathogenesis of intermittent exophthalmos. Arch. Ophth., **32**:1-10, 1944.

Weinberger, L. M., Adler, F. H., Grant, F. C.: Primary pituitary adenoma and the syndrome of the cavernous sinus: A clinical and anatomic study. Arch. Ophth., **24**:1197-1236, 1940.

Witt, J. A., McCarty, C. S., and Keating, F. R.: Craniopharyngioma (pituitary adamantinoma) in patients more than 60 years of age. J. Neurosurg., **12**:354-360, 1955.

Wyburn-Mason, R.: Arteriovenous aneurysm of mid-brain and retina, facial nevi and mental changes. Brain, **66**:163-203, 1943.

Wolfram, D. J.: Diabetes mellitus and simple optic atrophy among siblings. Proc. Staff Meet. Mayo Clinic, **13**:715-718, 1938.

Zondek, H.: On transient bitemporal hemianopsia (with report of a case associated with cerebellopontine diencephalic syndrome). Acta. med. orient (Tel-Aviv), **12**:102-106, 1953.

RETINOPATHY OF IMMATURITY*

In the newborn mouse after exposure to oxygen imbalances

Hedwige Habegger,† M.D., F. Randolf Philbrook, M.D., Francis J. Curley, and Theodore H. Ingalls, M.D.

Boston, Massachusetts

Introduction

This investigation was undertaken in order to compare normal retinovascular development in the newborn mouse with pathologic sequences provoked by disturbances of oxygenation. The mouse was selected for study because it is born prematurely by comparison with human beings—that is to say, the lids are undifferentiated and the eyes are "closed" like a puppy's or a kitten's. At birth the retina is immaturely developed and comparable to the retina of the markedly premature infant.[1,2] Both hyperoxia and hypoxia were used as stressing agents since experimental evidence indicates that both extremes of oxygen imbalance may produce retinopathies of the immature eye[3-6] and because much clinical evidence suggests that prolonged breathing of an atmosphere largely made up of oxygen may produce its injurious effect on the eye by first bringing about hypoxia.[7-13] This is the only hypothesis advanced to date that accounts for the development of retrolental fibroplasia in babies who have never been given oxygen therapy.[14-17]

Materials and Methods

The strain of white mice used in this study has been maintained in the laboratories of the Department of Epidemiology of the Harvard School of Public Health since 1947 on a standard diet of Purina dog-chow checkers with both food and water always available. During this time no outside mice have been introduced into the colony.

The provision of a normal atmospheric concentration of (20.9 percent) oxygen in

* From the Department of Epidemiology, Harvard University School of Public Health. Aided by grants from the Massachusetts Lions Eye Research Fund, Association for the Aid of Crippled Children, United Cerebral Palsy, and the American Heart Association.

† Helen Putnam Fellow, Radcliffe College.

room air and the creation of a high oxygen atmosphere within an incubator created no problems. For the latter purpose pure (U.S.P.) oxygen was piped through a bacteriologic incubator at a flow of about 6 liters per minute: and the temperature was stabilized at 23°C. In creating hypoxia, however, considerations of duration and degree of hypoxic stress were involved; procedures had to be worked out from the results of pilot experiments. As a first step newborn mice were exposed for five hours to a low pressure atmosphere to about 36,000 feet (10,970 meters) of altitude. These test animals were then replaced in a cage with litter mates as controls.

Since relatively acute hypoxia of this degree and duration had little detectable effect on the eye except that of causing transitory petechial hemorrhages, a second series of experiments were carried out which duplicated the hypoxic stress at daily intervals for several consecutive days. However, this procedure posed practical difficulties in maintaining and feeding and in decompressing and recompressing animals day after day. A simpler method for the creation of hypoxia was therefore sought.

A suitable apparatus was designed by Dr. John R. Suydam of Boston which employs two pyrex glass flowmeters (Corning No. 5960) mounted vertically on a plywood backboard for rigid support and connected by tubing to a plastic chamber. Air flows through one meter and dry nitrogen through the other. Thus oxygen may be diluted with nitrogen at normal atmospheric pressures until a desired concentration is reached. A third series of experiments was now conducted in an atmosphere of about 10-percent oxygen flowing through the chamber for days at a time.

In order to demonstrate vascular patterns within the retina three techniques were used: intracardiac injection of India ink and preparation of a flat retina after killing of the animal; opthalmoscopic examination of the fundus in animals that were studied in vivo; and the preparation of histologic sections stained with hematoxylin and eosin. For preparation of the injected flat retina pentobarbital-anesthetized mice were killed at daily intervals during the first two weeks of life and at three, four and six weeks thereafter. Intracardiac injection of India ink was made after the heart had been exposed, successful injection being manifested by the nose, ears, and lids turning black by the time the animal died. Fixation was in 10-percent formalin for 15 to 60 minutes depending on the age of the mouse. Before 14 days of age the skin of the head was removed, the closed lids were separated from the cornea, and 15 to 30 minutes of fixation sufficed; after eight days of age fixation required nearly 30 minutes. In older animals over 14 days of age the eyes were enucleated and placed in 10-percent formalin for an hour.

With corneal scissors, the anterior segment of the eye was separated from the posterior with the lens still attached to the optic stalk by the hyaloid vessels. The retina together with the lens was then dissected and lifted away from the choroid and the sclera. Four or more radial cuts were made in the retina to enable it to be flattened and the lens was cautiously manipulated, its relation to the retina being preserved.

A concavity slide was used to which Mayer's glycerin-albumin mixture had been applied one-half hour previously. After about five to 10 minutes the concavity was filled with a solution of 1.4 Dioxane (Eastman) for upward of an hour to dehydrate the retina. With an eye dropper this solution was removed and the excess absorbed with blotting paper. The preparation was next covered with Benzaldehyde for about 10 minutes to clear the retina and lens. Again free fluid was removed and excess blotted up with absorbent paper. The concavity was finally filled with Permount (Fisher) and covered with a glass cover-slide.

For funduscopic examination* of the eye it was necessary to anesthetize the mice with 0.04 to 0.06 cc. of 2.5-percent Nembutal depending on the age of the mouse. Mydriasis was obtained with the instillation of one drop of 0.5-percent cyclogyl (Schieffelin). Additional magnification of the fundus was obtained by means of a two-percent methyl cellulose drop placed directly on the cornea with the animal flat on its side in the examiner's hand so that no pressure was applied on the mouse's neck. This drop formed a contact lens which permitted opthalmoscopy as soon as the lids were opened at about two weeks of age. However, immediately after the eyes had "opened" ophthalmoscopic examination of the fundus was not satisfactory, and for a few days the fundus was only hazily discernible with a +10D. lens. Between the 16th and 17th days there was usually a marked change; the vitreous cleared and the fundus was distinctly seen with a +15 to +20D. lens. The examiner did not know which were the control and which were the test animals, thus making the funduscopy as objective as possible.

Results

Normal sequences

At birth the mouse retina in the strain studied is almost avascular. By the seventh day vascularization is observed to be basically complete, and vessels have reached the ora serrata in the sequence described below and shown in Table 1 where they are compared with those described for the human fetus.[1] During the period of vascularization in the mouse, the number of vessels emerging from the disc remains constant; from these vessels, especially the veins, retinal capillaries develop. A vein is not observed to cross an artery nor is there evidence of an avascular area corresponding to the macula of human beings.

The optic nerve, centrally placed and whitish, is not well outlined at any age and is more stellate than discoid. From this region the retinal arteries, thin and light red, diverge toward the periphery with relatively few ramifications; the veins are of larger diameter and of darker color. In young animals up to the age of about a month a whitish kind of granular tissue is discernible in the middle of the "disc" representing the visible remnant of the hyaloid system.

The pattern of developing blood vessels in the retina of the mouse at different ages is demonstrated in Figures 1 and 2 and described below:

Newborn mouse. A birth the hyaloid artery is well developed and its ramifications surround the lens with a vascular network. Several undifferentiated vessels proceed from the disc area toward the retina; they constitute a dense meshwork from which a few thin vessels diverge toward the periphery. These vessels appear to lie on the surface of the retina.

Two-day-old mouse. The hyaloid artery remains unchanged. The retinal vessels are still undifferentiated. However, the capillary network is formed of bigger meshes that have penetrated out toward the periphery of the retina.

Three-day-old mouse. The retinal vascular meshwork has extended still further and a few radial vessels begin to assume prominence. There is a definite difference in the caliber of these straight vessels; the smaller

* A surprising finding when ophthalmoscopic examination was first attempted was that one-half hour after instillation of two-percent neosynephrine, the lens was obscured by white cortical opacities preventing funduscopy. A cataractouslike process then developed to involve the whole lens within an hour. A two-percent solution of homatropine was substituted as a mydriatic but this too resulted in the production of a transient cataract slower in development and extension. In both cases the lens appeared to be transparent again 24 hours later when examined with a small hand slitlamp. These reversible opacities in the lens are interpreted as results of osmotic changes in the aqueous following the use of the mydriatic. Hertel[10] and Goldmann and Rabinowitz[11] described similar changes, the former after instillation of a strong saline solution and the latter by leaving the corneal surface exposed for several hours.

TABLE 1

SEQUENCES OF INTRAOCULAR VASCULARIZATION IN THE MOUSE AND IN THE HUMAN FETUS

	In the Mouse	In the Human Fetus
The arteria centralis retinae begins to branch on the disc	At birth	During the 3rd fetal month
The tunica vasculosa lentis begins to retrogress	At the 3rd–4th day	During the 4th fetal month
Retinal arteries and veins extend radially into the periphery and vertically into the deeper layers of the retina	From the 5th–8th day	During the 5th–6th fetal month
The main trunk of the hyaloid artery shrinks	At the 8th–10th day	During the 7th fetal month
Retinal vessels reach the ora serrata and the inner nuclear layer. Basic pattern of vascularization completed	At the 7th day	During the 8th fetal month
The hyaloid artery has involuted	At the 14th–18th day	During the 9th month

represent future arteries and the broader ones future veins.

Four-day-old mouse. Vascularization covers two thirds of the retinal surface. Arteries and veins may be easily distinguished from each other and between them capillary growth occurs. The vascular meshwork in the tunica vasculosa lentis has become looser and its meshes are wider. The hyaloid artery remains unchanged.

Five-to-six-day-old mouse. Arteries and veins are fully differentiated. Capillary extension is intensive near the periphery of the retina where small vessels are budding.

Seven-day-old mouse. The developing retinal vessels reach the ora serrata. Vessels in the tunica vasculosa lentis are undergoing slow regression.

Eight-day-old mouse. The entire retinal surface is now uniformly vascularized; no macula is discernible. Arteries and veins radiate from the disc area like spokes of a wheel. An artery is characteristically between two veins and the growth of capillaries appears to originate from veins. Around the arteries there is a free zone without capillaries, interrupted from place to place by an arteriole which ramifies and integrates with the capillary network of the adjacent vein. At the periphery the small vessels anastomose with capillaries of choroidal system.

Nine-day-old mouse. There is little change in the general vascular pattern of the retina. The hyaloid artery is shrinking.

Ten-to-12-day-old mouse. Six to eight arteries and veins emerge from the disc area; the number is relatively constant. The essential feature is in the still ramifying capillaries at the periphery that form a dense network between the main vessels.

Two-to-six-week-old mouse. Main vascular elements are all present and the retinal pattern is now that of an adult mouse; it remains unchanged in the older animal, except for general growth of the retina to keep pace with increase in size of the eye. Approximately six arteries each surrounded by two veins spread radially to the periphery and then ramify. These main vessels are connected by a dense capillary network, the meshes of which get smaller near the veins. The lens is free of vessels and the hyaloid artery has become reduced to a small remnant visible in the disc area.

SEQUENCES AFTER NEONATAL HYPOXIA

A single five-hour episode of hypoxia in the neonatal period produced preretinal hemorrhages more often in test animals than in controls. However, the numbers were small, the difference was one of degree rather than kind, and no permanent disturbances

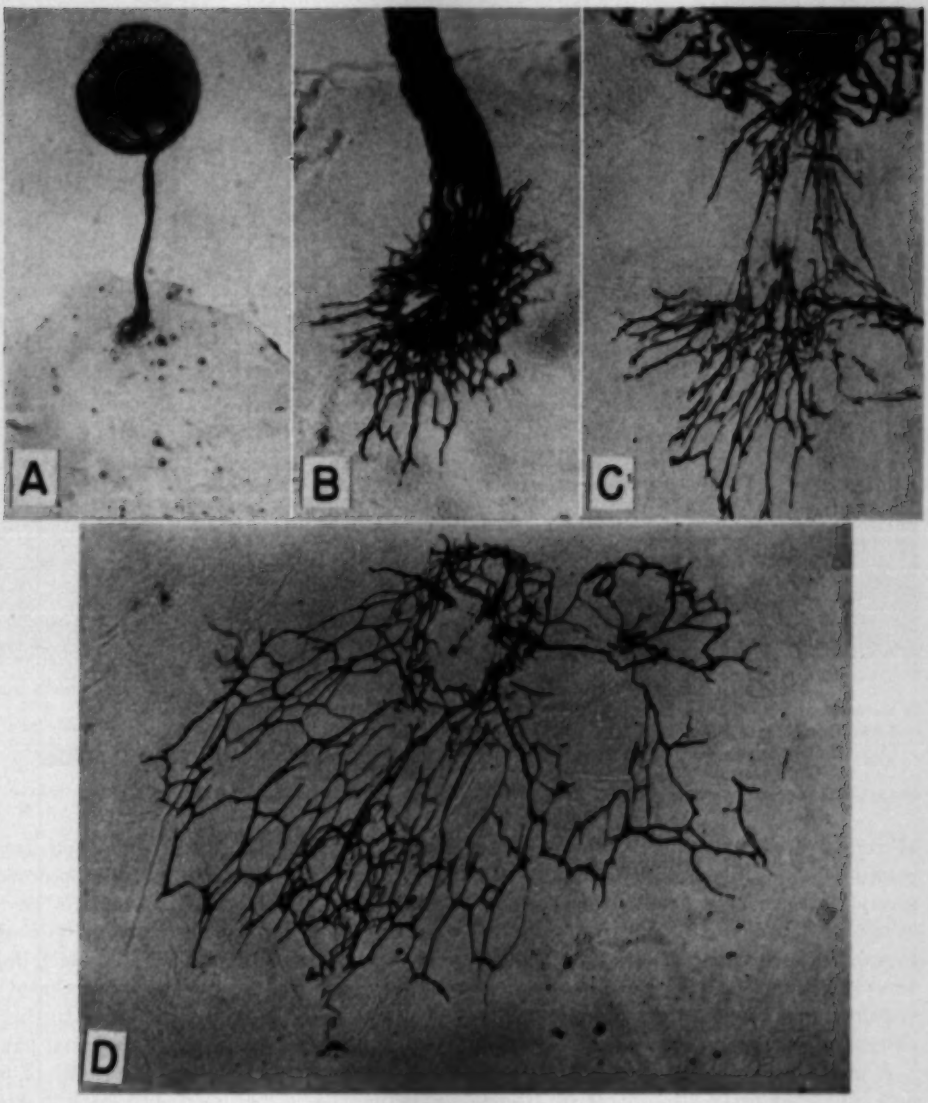


Fig. 1 (Habegger, Philbrook, Curley, and Ingalls). *Retinal vascularization in the mouse.* (India ink preparations.)

(A) Hyaloid artery and tunica vasculosa lentis of a newborn mouse (×24).

(B) Disc area of the same animal (×132).

(C) Disc area at two days of age (×80). The tunica vasculosa lentis is seen in the upper part of the photograph.

(D) Disc area at three days of age (×80).

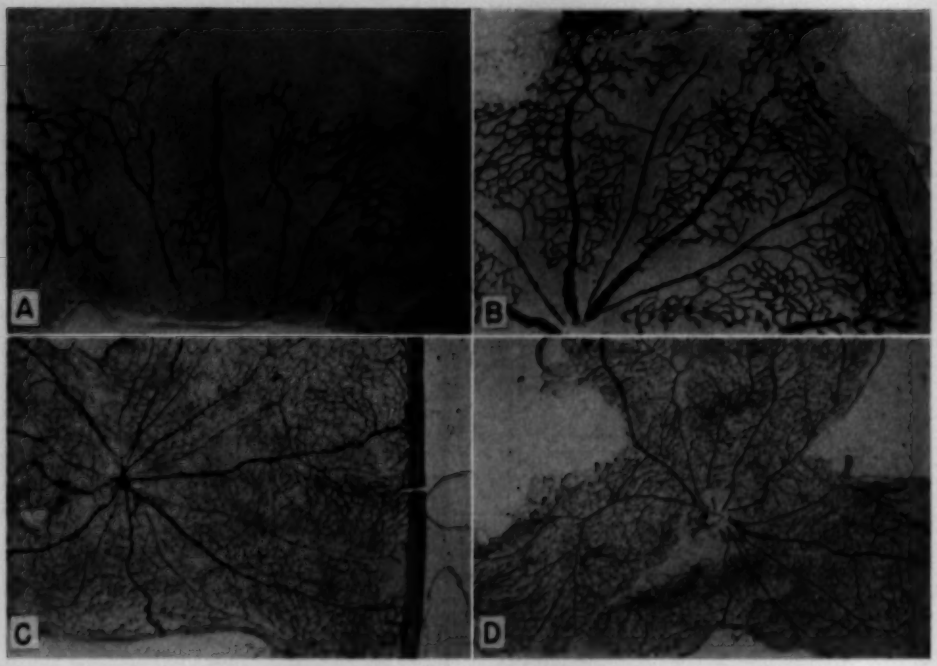


Fig. 2 (Habegger, Philbrook, Curley, and Ingalls). *Retinal vascularization in the mouse.* (India ink preparations.)
(A) At five days of age (×80).
(B) At eight days of age (×80).
(C) At 12 days of age (×34).
(D) Adult retinal pattern (×34).

of retinal architecture were observed. Repeated hypoxic stresses at daily intervals for several days produced definite retinal changes in two of eight animals studied, as shown in Figure 3. Such changes have not been observed in controls. However, it was with sustained hypoxia that the most satisfactory observations were made.

A litter of eight young mice five days old was submitted to an atmosphere of 10-percent oxygen at normal pressure for 48 hours and then removed to room air. On the 9th, 10th (figure 4-A), 17th, and 19th days of age, respectively, one animal was killed by injection of India ink together with a litter mate killed for histologic study. The injected retinas of these animals showed significant narrowing and distortion of retinal blood vessels.

Another litter of eight newborn mice two days of age was exposed to the same hypoxic atmosphere for four days. When six days old two were removed for study. One of these was injected with India ink which did not penetrate into the (presumably occluded) retinal vessels; the other was killed for histologic study which revealed abnormal vascularization of the vitreous (fig. 4-B). The experiment was continued until the 10th day of life when two more animals were killed for study purposes. One was injected with India ink which again failed to appear in the retinal circulation although aneurysmal dilatation of the hyaloid artery was observed (fig. 4-C). Histologically, the other showed persistence of hyaloid vessels in the vitreous and proliferation of the nerve-fiber layer.

The remaining four animals were allowed

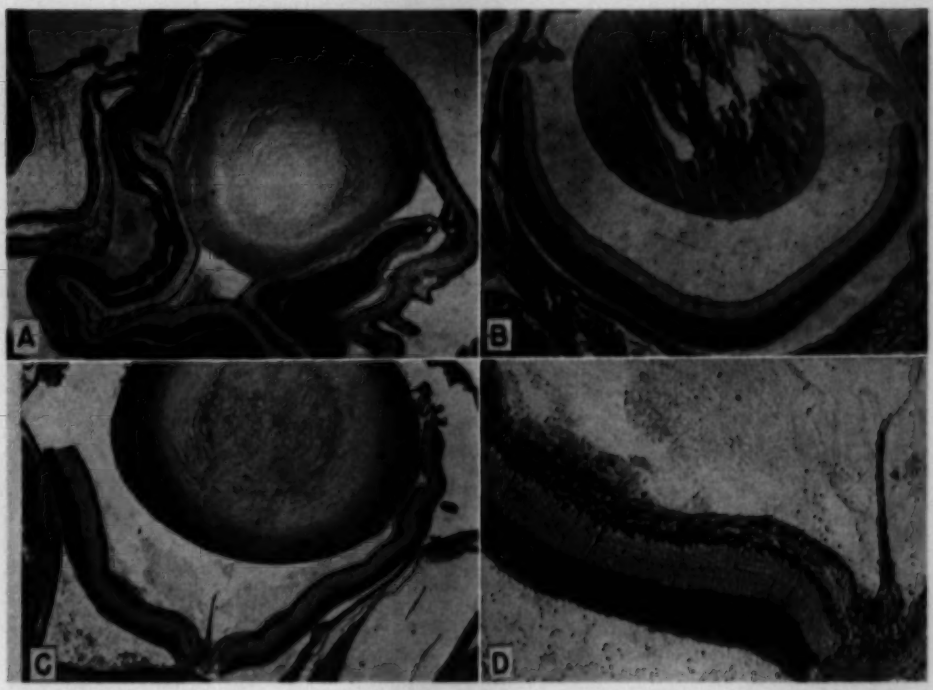


Fig. 3 (Habegger, Philbrook, Curley, and Ingalls). (A) Eye of a 26-day-old mouse exposed daily to a five-hour period of hypoxia from the fourth day of age and for nine days. The anterior chamber has disappeared and the lens is displaced forward in contact with the posterior surface of the cornea. The posterior capsule of the lens is ruptured in some places. The detached abnormal retina shows marked folding and is in contact with the lens. Cataractous changes are seen in the lens. (Hematoxylin-eosin ×46.)

(B) Eye of a 20-day-old control animal. The hyaloid artery has involuted. (Hematoxylin-eosin ×46.)

(C) Eye of a 24-day-old mouse exposed daily to five hours of hypoxia from the fifth day after birth and for seven days showing extravasation from persistent blood channels in the vitreous. The retina itself shows proliferation of the nerve-fiber layer. (Hematoxylin-eosin ×46.)

(D) Higher magnification (×160) of the nerve-fiber layer of the same animal shown in Figure 3-C.

to survive for five and one-half months by which time one was dead from unknown causes. Ophthalmoscopic examination of the remaining three showed retinal detachment in one, opacification of the lens with no retinal reflex in another, and a normal finding in the third. The two abnormal mice were killed for histologic study. Not only is the retina detached in both but an atrophy of all layers is present. No vessels are to be seen in the nerve-fiber layers; the vitreous space is markedly reduced and the lens shows cataractous changes (fig. 4-D).

Sequences after hyperoxia

Vasoconstriction of retinal vessels of persons breathing oxygen was reported by Cusick and his colleagues in 1940;[20] and in 1951 Campbell[21] showed by experiments on newborn rats kept in normal and hypoxic atmospheres that oxygen tensions in tissues around the vascular bed exert a significant influence on developing vessels. Budding capillaries grew toward loci of low oxygen tension. In 1954, Patz[22] observed persisting proliferative changes in the eyes of young rats, mice, kittens, and puppies after con-

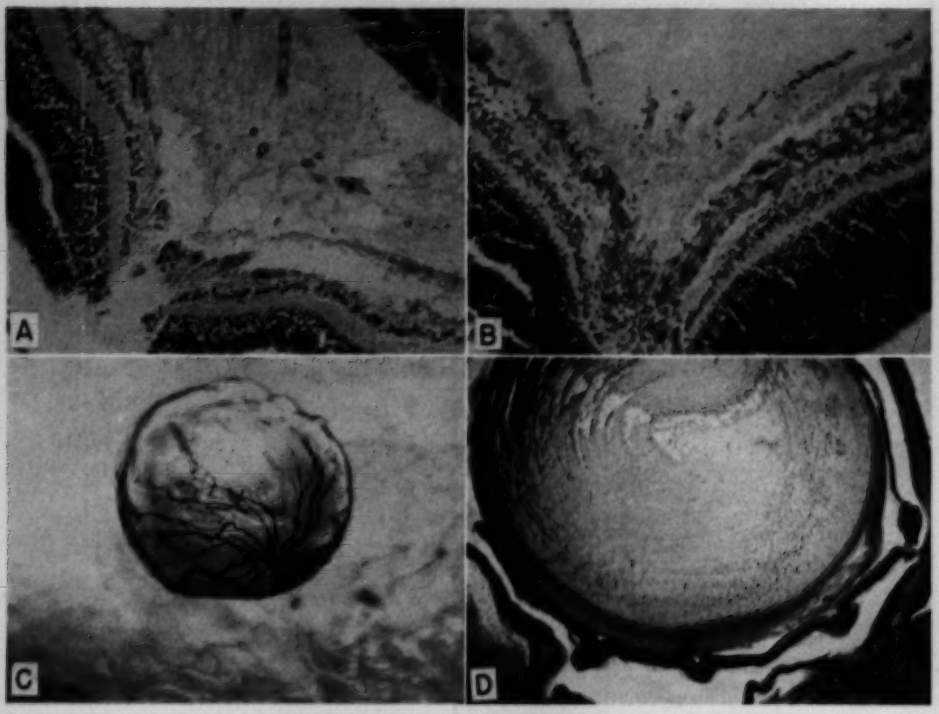


Fig. 4 (Habegger, Philbrook, Curley, and Ingalls). (A) Eye of a nine-day-old mouse exposed to an atmosphere of 10-percent oxygen from the second day after birth and for 48 hours. Persistent hyaloid capillaries are seen in the vitreous space. There is edema of the ganglion-cell layer. (Hematoxylin-eosin ×160.)

(B) Eye of a six-day-old mouse exposed to an atmosphere of 10-percent oxygen from the second day after birth and for four days. Excessive proliferation and penetration of neovascular tissue into the vitreous with extravasation is seen. (Hematoxylin-eosin ×160.)

(C) India ink injected eye of a 10-day-old mouse exposed to an atmosphere of 10-percent oxygen from the second day after birth and for eight days. Aneurysmal dilatation of the hyaloid artery has occurred at the posterior pole of the lens (×46). The retina appears out of focus in the background with no India ink-injected vessels discernible.

(D) Eye of a five and one-half month-old mouse exposed to an atmosphere of 10-percent oxygen from the second day after birth and for four days. An atrophic detached retina is adherent to the posterior capsule of the lens. (Hematoxylin-eosin ×46.)

tinuous exposure to an atmosphere high in oxygen for as long as 15 days. He observed that the residual hyaloid vessels which share a common union with the retinal vessels at the disc do not participate in the vasoconstriction. Under oxygen exposure instead of undergoing normal regression, the hyaloid vessels become dilated and undergo marked proliferation. Similarly the obliteration of retinal vessels of kittens was induced by Ashton and his colleagues[5, 23] as a manifestation of hyperoxia; and Gyllensten and Hellström[24] observed the hyaloid vessels to be dilated to an extent never seen in normal animals when oxygen was administered intermittently to newborn mice.

None of these investigators followed the evolution of retinal vascular disturbances week by week, evaluated them systematically by different lengths of exposure to hyperoxia, or by status of the lungs. Therefore the following experiment was designed for

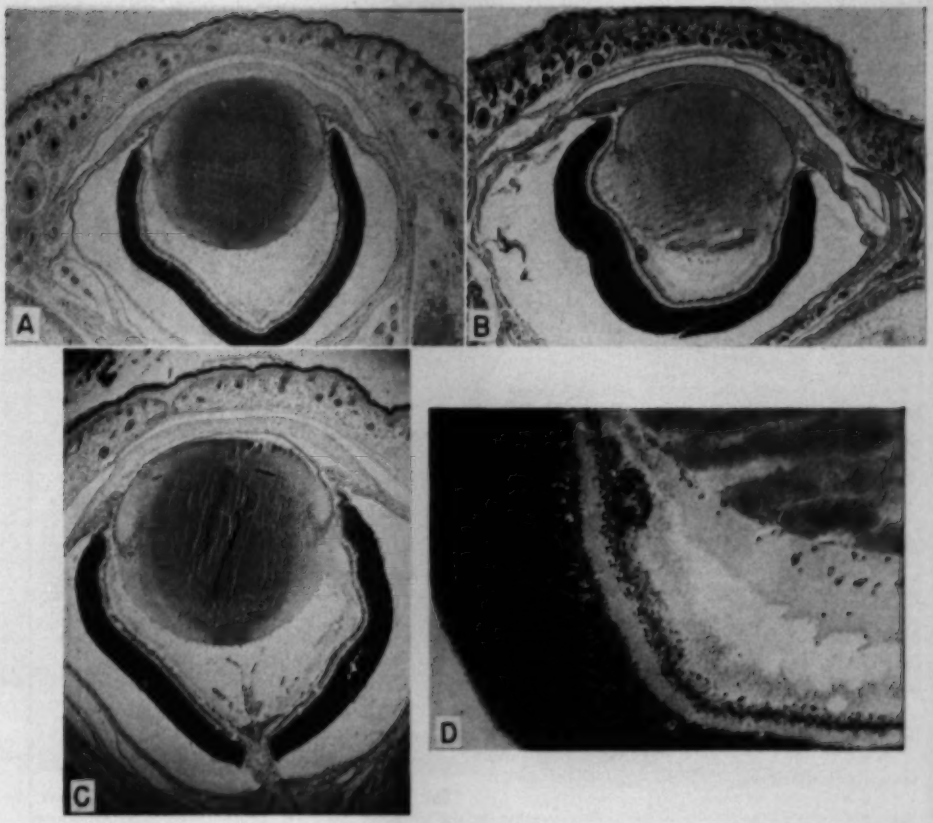


Fig. 5 (Habegger, Philbrook, Curley, and Ingalls). (A) Eye of newborn mouse in oxygen one day. The lids are still fused. Hyaloid vessels are well developed and no essential difference with the control is discernible. (Hematoxylin-eosin ×46.)

(B) Eye of a five-day-old mouse in oxygen since birth. Edema of the ganglion-cell layer and rosette formation and proliferation are seen in the nerve-fiber layer; there is extravasation of plasma into the vitreous. (Hematoxylin-eosin ×46.)

(C) Eye of a newborn control animal. (Hematoxylin-eosin ×46.)

(D) Rosette formation in the proliferating ganglion-cell layer of the mouse shown in Figure 5-B (×160).

newborn mice breathing pure oxygen (U.S.P.) since birth. After 3, 5, 7, 9, 13, 20, and 28 days, respectively, of exposure, one of the young was killed for histologic study of the eye and of the lung. A control litter of eight animals was killed on a similar time-schedule so that normal sequences— especially of the regression of the hyaloid artery system—could be compared. Figures 5, 6, 7, and 8 illustrate the results.

Dilatation of the hyaloid vessels was not seen in very young animals before a week's exposure to high oxygen tension; it was beginning to be evident in those killed before two weeks. Progressive dilatation of the type reported by others, developed during the second week of exposure, and gradually increased to a maximum on the 28th day when there was marked dilatation of the vessels at the posterior surface of the lens, in the

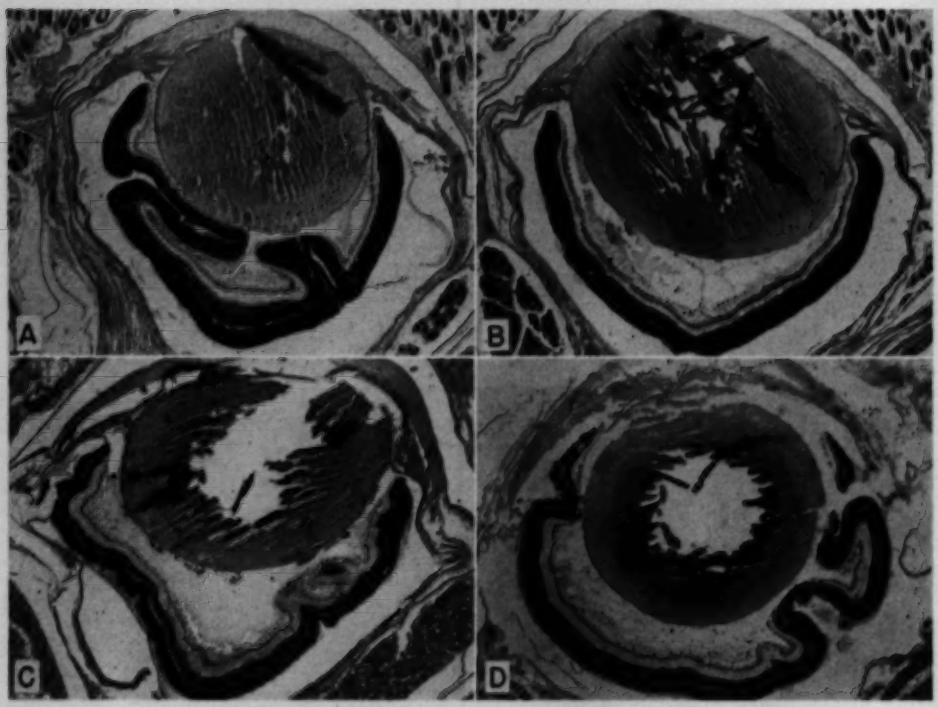


Fig. 6 (Habegger, Philbrook, Curley, and Ingalls). (A) Eye of a seven-day-old mouse in oxygen since birth. There is retinal folding and proliferation of the nerve-fiber layer. (Hematoxylin-eosin ×46.)
(B) Eye of a seven-day-old control. The retina is differentiated into three nuclear layers. Hyaloid vessels are involuting. (Hematoxylin-eosin ×46.)
(C) Eye of a 13-day-old mouse in oxygen since birth. Proliferation of the nerve-fiber layer and persistent dilated hyaloid vessels and extravasation in the vitreous are seen. (Hematoxylin-eosin ×46.)
(D) Eye of a 13-day-old control (×46). The nerve-fiber layer is well differentiated.

primary vitreous body, in the iris stroma, and at the posterior surface of the iris (fig. 7-C and D). Proliferative changes in the retina and neovascular responses were marked at four weeks of age when the experiment ended.

Findings were consistent with the concept of a localized manifestation of gradually increasing "oxygen poisoning" and hypoxia as described by Pichotka[25] and Becker-Freyseng[26] and confirmed by Bruns and Shields.[27] However, the pulmonary manifestations in these young animals were different from those described in older animals (hyaline degeneration of capillaries and pulmonary hyaline membrane) by Pichotka. Histologic sections of the lungs showed vascular engorgement, septal hemorrhages, and perivascular edema. Some hyaline degeneration of the walls of small arteries was observed but without pulmonary hyaline membrane formation in the alveoli (fig. 8). After the end of the second week there was a gradual return of lung structure toward normal, probably representing adaptation. In any event newborn animals neither died nor developed the necrosis of alveolar sacs to be found at later ages; they did develop early retrolental fibroplasia as has been described by others.

Discussion

Research of the early 1950's gradually but conclusively implicated oxygen poisoning as the principal cause of retrolental fibro-

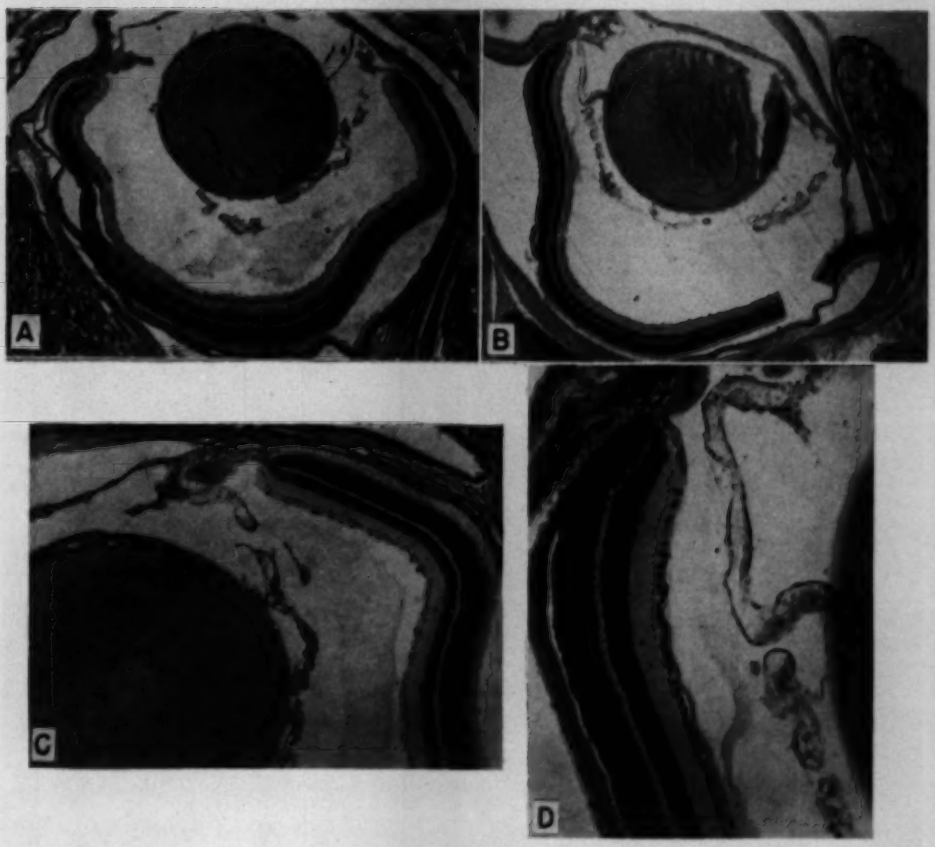


Fig. 7 (Habegger, Philbrook, Curley, and Ingalls). (A) Eye of a 20-day-old mouse in oxygen since birth. Marked congestion of the iris vessels and dilated vessels in the vitreous are seen. (Hematoxylin-eosin ×46.)

(B) Eye of a 28-day-old mouse in oxygen since birth. Marked congestion of the iris vessels and dilated vessels behind the lens are evident. (Hematoxylin-eosin ×46.)

(C) Eye of a 20-day-old mouse in oxygen since birth. Marked dilatation of the vessels at the posterior surface of the lens and iris and extravasation into the vitreous are to be seen. (Hematoxylin-eosin ×160.)

(D) Eye of a 28-day-old mouse in oxygen since birth. There is marked congestion and dilatation of the persistent hyaloid vessels. (Hematoxylin-eosin ×160.)

plasia. However, the physicochemical mechanism producing the ocular condition has never been clarified and a baffling feature is that hyperoxia ultimately produces many of the symptoms associated with oxygen want; these symptoms are precipitated when the infant is abruptly removed from the incubator.

In 1951, Szewczyk observed that prompt congestion of the veins in the eyegrounds and signs of hypoxia occurred in seven premature infants previously maintained in 50-percent oxygen when they were removed to room air, whereas the vessels of nine infants with early signs of retrolental fibroplasia became less congested when the babies were placed in a high oxygen atmosphere. Congestive changes were interpreted to have been caused by withdrawing babies so rapidly that a relative hypoxia was induced. This

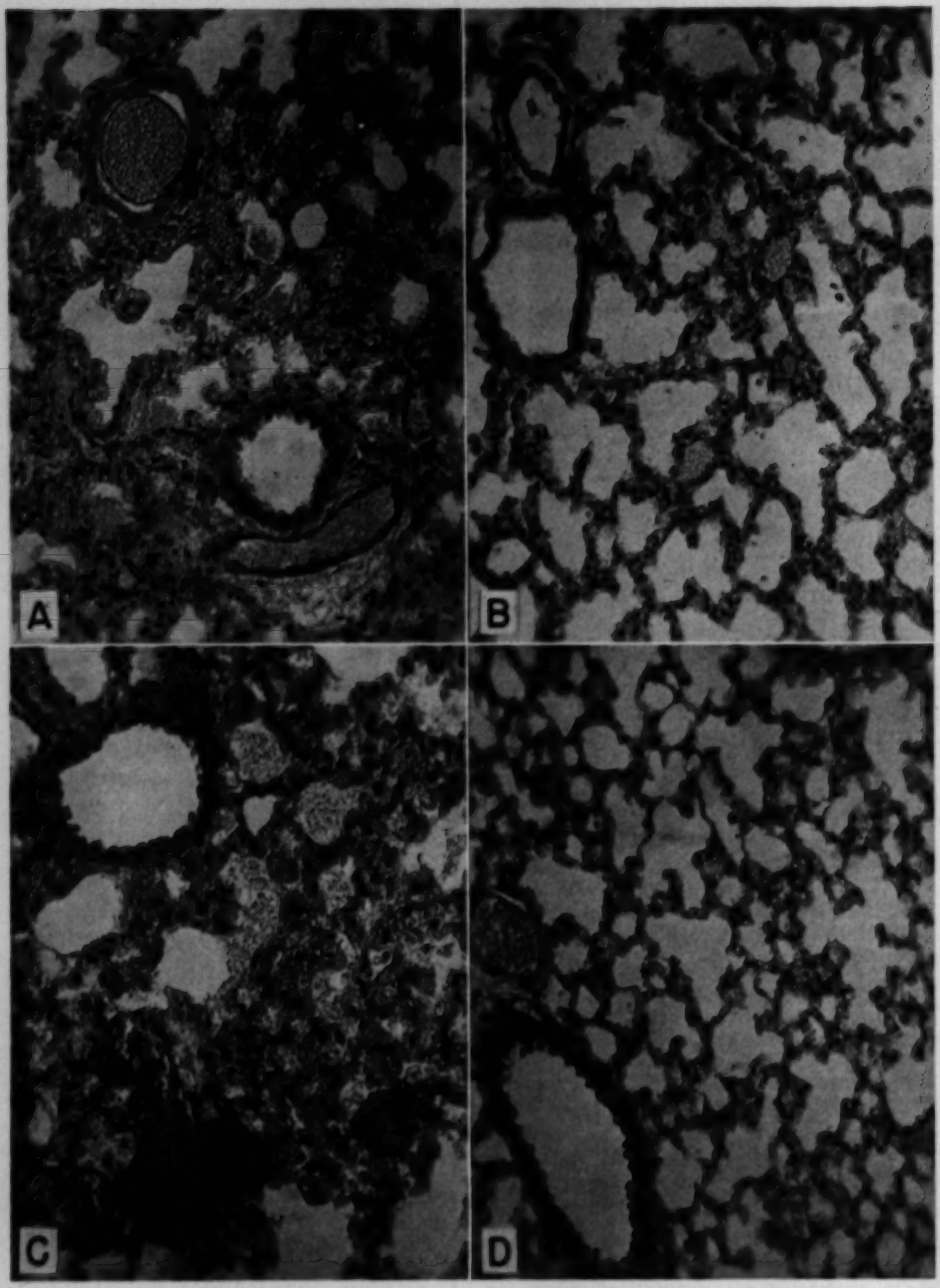


Fig. 8 (Habegger, Philbrook, Curley, and Ingalls). (A) Lung of a five-day-old mouse in oxygen since birth. Congestion with intra-alveolar and septal hemorrhage and hyalinosis of walls of small vessels are evident. (Hematoxylin-eosin ×200.)

(B) Lung of a five-day-old control animal. (Hematoxylin-eosin ×200.)

(C) Lung of a 13-day-old mouse in oxygen since birth showing congestion and perivascular edema. (Hematoxylin-eosin ×200.)

(D) Lung of a 13-day-old control. (Hematoxylin-eosin 200×.)

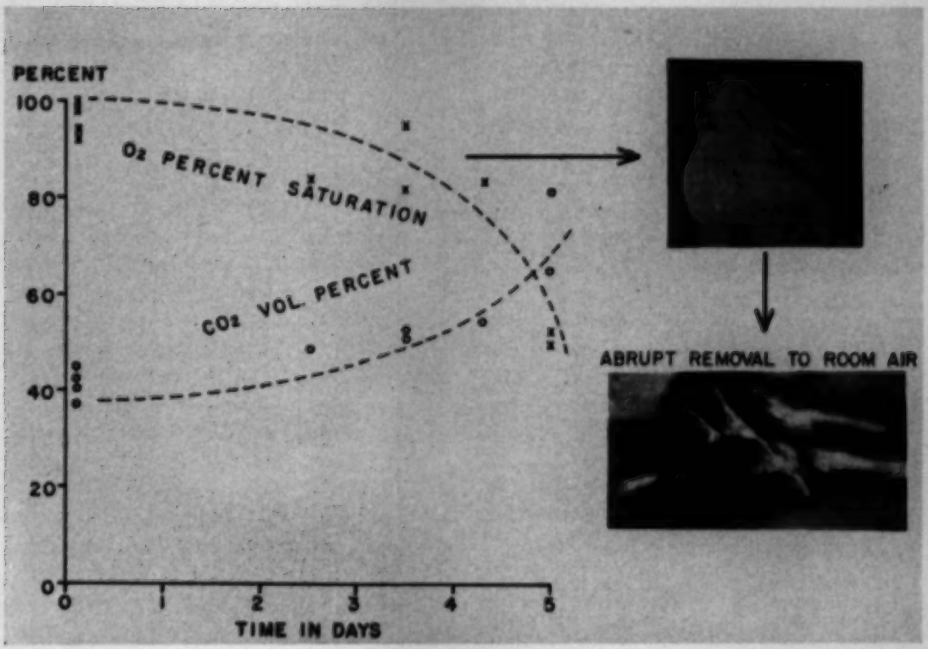


Fig. 9 (Habegger, Philbrook, Curley, and Ingalls). Synopsis of four experiments on rabbits maintained in oxygen at one atmosphere of pressure for five days. There is a progressive decrease in the oxygen saturation of the blood and rise in its carbon-dioxide combining power. (Source: Becker-Freyseng.[38])

general experience has been confirmed by Jefferson and by Bedrossian and his coworkers. Even more provocative are the six cases of retrolental fibroplasia that have been reported in infants who have never been given oxygen therapy.

Experimentally, the problem of oxygen toxicity at normal atmospheric pressures was approached by Becker-Freyseng as part of German (World War II) aviation research. Following exposure to oxygen at one atmosphere of pressure he demonstrated a progressively diminishing oxygen saturation of the blood and a progressive rise in its carbon dioxide content with each day that rabbits were maintained in the purified gas. Figure 9 presents synoptically the results of four of his experiments and also portrays the sudden collapse of the animal when abruptly removed to room air after four to five days' oxygen. At advanced stages of pulmonary embarrassment it is Becker-Freyseng's interpretation that oxygen "acts simultaneously as a poison and as a therapeutic agent."

The explanation for this kind of behavior in the adult animal was thought to lie in the pulmonary hyaline membrane which formed as a reactive process to the breathing of oxygen. The association appears to be well established for adult animals; but physicians confronted with retrolental fibroplasia are concerned with disturbances of immature organs. The factor of age—particularly as it relates to the development of the eyes and the lungs—needs to be taken into account when the pulmonary systemic and ocular consequences of prolonged breathing of air high in oxygen content are studied.

The newborn mouse is well suited for study of aging factors and it has proved possible to follow the development of retinal vessels from mere buds at birth to the mature pattern evident at two weeks of age. The normal process may be likened to the

construction of a spider web of radiating arterioles and connecting capillaries starting from the center and working outward in ever widening circles.

At one week of age in the strain studied the radiating vessels are generally reaching the ora serrata and the retina itself is undergoing active differentiation into the three nuclear layers to be found in the adult eye. By two weeks of age connecting capillaries and vessels have appeared and the basic vascular pattern is that of the adult animal.

The first week or two after birth is thus a critical period for retinal vascularization. It is a time when gross retinopathy might be expected to result from significant injury to the blood vessels whether that be produced by hypoxia, hyperoxia, or other stress. Blighting of the retinal circulation and disruption of retinal structure were in fact induced as late manifestations of acute imbalances at this period.

The most pronounced disturbance followed daily hypoxic stresses during the second week of life but the pathologic changes induced by both hyperoxia and hypoxia were remarkably similar to each other. Abnormal congestion, persistence, and proliferation of the branches of the hyaloid artery system could be demonstrated after each kind of injury providing it was severe enough in intensity and prolonged enough in duration in the neonatal period. A few episodes of sustained hypoxia sufficed to produce residual lesions of the retina, whereas at least five days of hyperoxia were required to produce a comparable result.

The experimental sequences indicated clearly that vascular disturbances underly the retinopathy, and that the precise nature of these disturbances depends among other factors on the stage of growth reached by the retinal vessels and the degree of involution attained by the hyaloid vessels at the time critical stress occurred.

Development of the lungs was not followed in as detailed a manner as was development of the eyes. However, the limited observations that were made throw some light on the main points which are today at issue—whether atmospheric hyperoxia produces hypoxia in young animals as it does in adults and, if so, whether this be through a series of pulmonary changes or by impaired oxygenation of the blood.

For many years physiologists have been in general agreement that the pulmonary changes produced in older animals breathing oxygen at atmospheric pressure ultimately result from anoxia. The sequences leading to oxygen want in the midst of oxygen are so clearly evident that Binger, Faulkner, and Moore in 1927 referred to the state as "hyperoxic anoxia.[28] The concept was confirmed and expanded by Bean and Bohr[29] in 1940.

The results of our experiments are in harmony with the concept that hyperoxic hypoxia may also be induced in the neonatal period and that it comes about through some mechanism other than pulmonary irritation and reaction. Newborn mice exposed from birth to an atmosphere of oxygen showed a progressively increasing congestion of the lung previous to intraocular vascular changes; but they did not die as did older mice; nor did they show pulmonary hyaline membranes when killed. After four weeks of sustained hyperoxia when the experiment was discontinued, the eyes revealed a distinctively pathologic vascular pattern, whereas the lungs showed a "recovered normal" structure.

There are evidently age-specific factors determining resistance to hyperoxia which are characteristic of newborn mice, just as there are factors that give increased resistance to hypoxia in the neonatal period. What these factors are is a matter of speculation and further research. A significant difference between the very young and adult rats and mice is implicit in the fact that adults exposed to oxygen do not live long enough to develop chronic disturbances of the retina—or any other organ.

The similarity if not the identity of the

vascular abnormalities brought about by hyperoxia or hypoxia strongly suggests that they have a final common mechanism; this would seem to be hypoxia. The suggestion finds support in the capacity of newborn mice to outlive adults in either a hypoxic or hyperoxic atmosphere.

In explanation of the facts, pressure changes are a first consideration, for the decreased oxygen tension found at high altitudes is a gradientlike affair, changing gradually as the organism approaches sea level. Pursuing the analogy of a continuing descent from Mt. Everest to sea level and as far again below, it may be calculated that to place an infant in 60-percent oxygen is equivalent to descending some six miles below sea level in terms of density of oxygen molecules breathed.

The analogy ignores, of course, factors other than oxygen tensions that are also decisive homeostatic considerations—pH of the blood, hematocrit, hemaglobin, and blood count; environmental and body temperatures; dissolution of oxygen at high tensions in the serum and tissues; and caliber changes of blood vessels which Ashton, Ward, and Serpell, and Kerr and Scott felt were important. The analogy given merely illustrates the complex role played by a single factor, oxygen tension; and it dramatizes the extreme nature of physiologic shifts that were not often taken into account by clinicians and nurses administering oxygen therapy.

Summary and Conclusions

Retinopathies of immaturity may be initiated by either hyperoxia or hypoxia—probably by a common mechanism: hypoxia. The stage of retinal vascular development, when oxygen imbalance occurs, as well as its degree, duration, repetition, and changing character, may determine the end result.

The results of these experiments support a concept of retrolental fibroplasia as a late manifestation of oxygen want during the fetal period of development. In this regard, it is pertinent that the early manifestations of retrolental fibroplasia are dilatation and tortuosity of retinal vessels and frequently retinal hemorrhages. The signs are those of hypoxia; the practical demonstration is the necessity for a balanced oxygen supply.

The clarification of retinal malformations brought about in the past decade bears directly on the genesis of congenital anomalies. Retrolental fibroplasia, for example, is essentially a congenital defect in the sense that it develops at a time when the infant should be residing in utero. No doubt the cerebral palsy and electroencephalographic changes that have been frequently reported to accompany retrolental fibroplasia have a corresponding kind of "congenital" pathogenesis in that part of the vascular system which nourishes the cerebral cortex. When such disorders have their onset during pregnancy, the only way that the pathogensis can be reconstructed is by inference from experimental, clinical, and epidemiologic observations. When the ocular defect has its onset after birth, the observer is in the position of being able to watch the genesis of a congenital defect by direct inspection.

One Shattuck Street (15).

References

1. Mann, I.: The Development of the Human Eye. New York, Grune & Stratton, 1950, ed. 2, p. 228.
2. Fletcher, M. C.: The developing fundus oculi of the premature infant and its relationship to retrolental fibroplasia. J. Pediat., **43**:499-523, 1953.
3. Ingalls, T. H., Tedeschi, C. G., and Helpern, M.: Congenital malformations of the eye induced in mice by maternal anoxia; with particular reference to the problem of retrolental fibroplasia in man. Am. J. Ophth., **35**:311-329, 1952.
4. Patz, A., Eastham, A., Higginbotham, D. H., and Kleh, T.: Oxygen studies in retrolental fibroplasia: II. The production of the microscopic changes of retrolental fibroplasia in experimental animals. Am. J. Ophth., **36**:1511-1522, 1953.
5. Ashton, N., Ward, B., and Serpell, G.: Effect of oxygen on developing vessels with particular reference to the problem of retrolental fibroplasia. Brit. J. Ophth., **38**:397-432, 1954.

6. Gyllensten, L. J., Hellestrom, B. E.: Retrolental fibroplasia: Animal experiments: The effect of intermittingly administered oxygen on the postnatal development of the eyes of full term mice: A preliminary report. Acta paediat., **41**:577-582, 1952.

7. Szewczyk, T. S.: Retrolental fibroplasia: Etiology and prophylaxis: A preliminary report. Am. J. Ophth., **34**:1649-1650, 1951.

8. ———: Retrolental fibroplasia: Etiology and prophylaxis. Am. J. Ophth., **35**:301-311, 1952.

9. Jefferson, E.: Retrolental fibroplasia. Arch. Dis. Child., **27**:329-336, 1952.

10. Bedrossian, R. H., Carmichael, P., and Ritter, J.: Retinopathy of prematurity (retrolental fibroplasia) and oxygen. Am. J. Ophth., **37**:78-86, 1954.

11. Ingalls, T. H., and Purshottam, N.: Oxygenation and retrolental fibroplasia. New England J. Med., **250**:621-629, 1954.

12. Ingalls, T. H.: Epidemiology of retrolental fibroplasia: Its etiologic relation to pulmonary hyaline membrane. New England J. Med., **251**:1017-1022, 1954.

13. Ingalls, T. H., Minkowski, A., and Bourgonnier, L.: Rétinopathie des prématures et oxygénation, Courrier, **4**:475-480, 1954.

14. Bembridge, B. A., Coxon, M., Houlton, A. C., Jackson, C. R. S., and Smallpiece, V.: Retrolental fibroplasia: A problem of prematurity. Brit. Med. J., **1**:675-680, 1952.

15. Kerr, J. D., and Scott, G. I.: The retinopathy of prematurity. Arch. Dis. Child., **29**:543-550, 1954.

16. Pico, G.: Retrolental fibroplasia: Three cases in Puerto Rico, Bol. assoc. med., Puerto Rico, **47**: 288-296, 1955.

17. Yankauer, A., Jacobziner, H., and Schneider, D. M.: The rise and fall of retrolental fibroplasia in New York State: Preliminary report. New York State J. Med., **56**:1474-1477 (May) 1956.

18. Hertel, E.: Experimentelle Untersuchungen über die Abhängigkeit des Augendruckes von der Blutbeschaffenheit. Arch. f. Ophth., **88**:197-229, 1914.

19. Goldmann, H., and Rabinowitz, S.: Ueber eine unbekannte reversible Kataraktform bei jungen Ratten, Klin. Monatsbl. f. Augenh., **81**:711-785, 1928.

20. Cusick, P. L., Benson, O. O., and Boothby, W. M.: Effect of anoxia and of high concentrations of oxygen on retinal vessels: Preliminary report. Proc. Staff Meet., Mayo Clinic, **15**:500-502, 1940.

21. Campbell, F. W.: Influence of low atmospheric pressure on development of retinal vessels in rat. Tr. Ophth. Soc. U. Kingdom, **71**:287-300, 1951.

22. Patz, A.: Oxygen studies in retrolental fibroplasia. IV. Clinical and experimental observations. Am. J. Ophth., **38**:291-308, 1954.

23. Ashton, N., and Cook, C.: Direct observation of the effect of oxygen on developing vessels. Preliminary report. Brit. J. Ophth., **38**:433-470, 1954.

24. Gyllensten, L. J., and Hellström, B. E.: Experimental approach to the pathogenesis of retrolental fibroplasia: I. Changes of the eye induced by exposure of newborn mice to concentrated oxygen. Acta paediat., **43**:(supple. 100) 131-148, 1954.

25. Pichotka, J.: Morphology and morphogenesis of pulmonary changes due to oxygen poisoning. Department of the Air Force. German Aviation Medicine, World War II, **1**:515-525, 1950.

26. Becker-Freyseng, H.: Physiological and patho-physiological effects of increased oxygen tensions. Department of the Air Force. German Aviation Medicine, World War II, **1**:493-514, 1950.

27. Bruns, P. D., and Shields, L. V.: High oxygen and hyalinelike membranes, Am. J. Obst. & Gynec., **67**:1224-1236, 1954.

28. Binger, C. A. L., Faulkner, J. M., and Moore, R. L.: Oxygen poisoning in mammals. J. Exper. Med., **45**:849-864, 1927.

29. Bean, J. W., and Bohr, D. F.: Anoxic effects of high oxygen pressure on smooth muscle. Am. J. Physiol., **130**:445-453, 1940.

HAWAII THROUGH THE OPHTHALMOSCOPE

WILLIAM JOHN HOLMES, M.D.
Honolulu, Hawaii

The Hawaiian Archipelago is a group of islands, reefs, and shoals strung out from the southeast to the northwest for 1,600 miles between 154° 40′ and 178° 75′ W. longitude and 18° 50′ N. latitude.[1] Due to the postion of the islands in the Pacific Ocean, the influence of the drift of ocean currents and trade winds from the northeast, the climate is considered subtropical. It is not subject to violent atmospheric disturbances, typhoons, or hurricanes. The average annual temperature varies from a low of 60° F. to a high of 84° F. The relative humidity remains comparatively constant at 70 percent. Barometric variations compared to those in the mainland United States are negligible. The wind velocity is, however, quite high averaging 8.6 miles per hour (756 feet per minute) with east or a northeast wind prevailing. The average rainfall is approximately 25 inches per year. Due to the mountainous topography, the amount of rain that falls varies widely within very short distances. Population of the Territory is 476,913.* The people of Hawaii by racial antecedents are made up of Hawaiians and part-Hawaiians, Japanese, Caucasians, Filipinos, Chinese, Koreans, Puerto Ricans, and mixtures of these races. The Hawaiian Islands represent a melting pot of races which blend happily together at work and play.[2]

CIVILIAN POPULATION BY RACE[1]

All Races	476,913
Hawaiian	12,108
Part Hawaiian	73,483
Caucasian	95,331
Chinese	32,225
Japanese	184,119
Filipino	60,453
Puerto Rican	8,852
Korean	6,492
All Other	3,850

* Based on 1950 Bureau of Census report, as of April, 1950.

HOSPITALS

There are 38 hospitals in the Territory of Hawaii, registered with the Board of Health. There is also one large army—Tripler—hospital for military personnel, their dependents, and veterans.

LANGUAGE

The language of Hawaii as a Territory of the United States is English. Yet, as a time-saving measure in talking with some of my elderly Oriental patients, the translations in Table 1, hung on the wall of one of my examining rooms, have been very useful.

RACIAL DIFFERENCES

The Territory of Hawaii with its mild, pleasant, subtropical climate, its multiracial, nonmigrant population, theoretically offers an ideal laboratory for the investigation of racial and genetic factors that bear on diseases of the eye. However, due to the high standards of living by the first-generation settlers from Asia, the gradual adoption of typical American living habits by second and third generations, along with the frequency of intermarriage between the various races, it is difficult to draw valid racial generalizations. Nevertheless, a few of the older first-generation settlers from the Orient and the Pacific isles still adhere to some of the traditions, tribal and dietary customs, religious rites, and health habits of their forebears.

Of special ophthalmologic interest among the various races are some of the following:

PHYSIOGNOMY

According to Martin,[3] the breadth of the palpebral fissure averages 26.6 mm. in the Chinese, 28.9 mm. in the Japanese, and 32.9 mm. among the Greeks. In oriental children and even in some adults wide epicanthus,

TABLE 1

TRANSLATION CHART FOR PATIENTS LIVING IN HAWAII

	Hawaiian	Japanese	Chinese	Korean	Filipino
Open your eyes	Hemo ka maka	Akenasai	Hoy ngan	Noon thu say yo	Buksan mo ang mata mo
Close your eyes	Pae ka maka	Tsumenasai	Sarn ngan	Noon tar chi say yo	Sara mo ang mata mo
Look up	Nana iluna	Ue minasai	Horn Kau	Char jar boh say yo	Tumingin ka sa itaas
Look down	Nana ilalo	Shita minasai	Horn dai	Ah lay boh say yo	Tumingin ka sa ibaba
Do not squeeze your eyes	Aole hana ka maka a paa loa	Kataku shime-naide	Um hau ja ngan	Noon ool kharm par har ji mar say yo	Huag mo isara any mata mo mabuti

the so-called oriental or "mongoloid" fold may simulate convergent squint. Apparent asymptomatic trichiasis and entropion are also occasionally encountered among oriental children. They are due to a peculiar arrangement of the lower part of the orbicularis oculi muscle, whereby, as seen in sagittal section, marginal fibers are disposed backward in a curve or even kink.

Another fairly common anatomic finding among oriental people is the congenital absence of an upper lid fold. From time to time, but especially during World War II, young Hawaii-born Japanese adults consulted ophthalmic surgeons to provide them with such a fold in order to "westernize" their oriental eyes.

Such an operation described and advocated by Sayoc[4] consists of a "horizontal incision across the upper lid. The incision cuts through the skin, subcutaneous tissue, and orbicularis. A narrow, one- to two-mm. strip of orbicularis is then removed, and the lower skin flap is anchored to the anterior surface of the exposed tarsus. The incision is closed with 4-0 black silk, interrupted sutures."

The low nasal crest bordering on the virtual absence of this crest among oriental people often requires the application of adjustable nose pads and arms to their glasses or goggles. The flat oriental nose brings to mind a patient for whom a nasal prosthesis attached to a pair of glasses was ordered. True-to-life Kodachrome photographs and a plaster-of-paris mold of the face were sent to the manufacturer. The finished product was a perfect fit, but the patient refused to wear it, as the prosthesis was a straight Roman nose. When it was returned and exchanged for a flat, oriental type of nose with a sunken nasal crest, the patient happily accepted it and to this date continues to wear it.

ERRORS OF REFRACTION

Crawford and Hamman[5] reported on the refractive errors of 8,819 school children from kindergarten through high school. They found myopic errors more frequently among students of oriental extraction. The Chinese led both the Japanese and Korean groups. The authors suggest that this finding may be ascribed to the age of the oriental civilization and culture since the more primitive races, such as Hawaiian, part-Hawaiian, and Filipino had less myopia with the Caucasian groups in between.

Filipinos develop presbyopia at an earlier age than orientals or Caucasians. A similar observation was made by Rambo[6] among the Hindus.

Night vision

During World War II, comparative tests of photopic and scotopic vision between 217 Japanese and Caucasian students were carried out.[7] These tests revealed a higher racial incidence of myopia and myopic astigmatism (28.11 percent) among the Japanese than the Caucasian group (5.07 percent). The Japanese group as a whole did also more poorly on each of six tests for night vision than the Caucasian group. These differences were ascribed to hereditary factors, to the greater frequency of myopia among the Japanese, the possible inadequate dietary intake of vitamins A and B in the Japanese diet, and an abnormal ratio of calcium and phosphorus in the Japanese diet.

Glare

Visible light, reflected from coral, sand, surf, water, and clouds may be sufficiently bright to cause glare.

Tinted lenses with 10- to 25-percent[8] transmission have been found effective in Hawaii to reduce the brightness to optimum levels for vision.

Racial beliefs and ancient customs

Hawaiian

I'ooi na lihilikamaka. To "sharpen the eyelashes" of a newborn baby, hide his afterbirth in the hollow of a young pandanus. Just as the tree has sharp thorns so the eyelashes and brows will become sharper and give the eyes a bright, sharp look.[9]

*Treatment for Sore Eyes**

1. Feed the tender, unopened leaf bud of the breadfruit tree together with the honualoa variety of sugar cane. If the patient becomes aware of a sensation of numbness, his sore eyes will improve.

2. Squeeze the juice of puakala and let it drop into a large shell. Blend it with human mother's milk and place upon the eye.

3. Sprinkle the eye with cold water five times a day.

4. Gather 20 auhuhu flowers. Chew well, then blow it into the patient's eyes five times.

5. Pick some kekaepuaa grass; chew well, then blow it into the patient's eyes five times.

6. Ti leaf is another remedy. Use a ripe leaf for men and a green leaf for women. Shred the ribs into little pieces; chew until smooth, and form into little balls. While the patient lies quietly, in a prone position, close his eyelids and place the balls upon his eye sockets. On the second application, also have him roll his eyeballs five times.

7. Early in the morning, roll your eyes three to five times in the trough from which cows drink water. The cows' saliva after they chew certain grasses is believed to cure sore eyes.

Treatment for Cataract in the Eye

(This probably refers to pterygium)

Cataracts, according to Handy, Pukui, and Livermore,[10] were treated as follows:

Gently scrape the surface of the cornea with a bit of silk-soft kapa, soft kukæ puaa grass, or soft sweet potato leaf, rolled in the fingers. Following this operation, drop the juice of papolo into the inflamed eyes. As an alternative, blow kukæ puaa from your mouth upon the eyeball.

Samoan

Bathe the eyes in fresh pool of water (not in the ocean). Blow at the eyes of the afflicted. This will blow away the sickness.

Chinese

1. Wash the infant's eyes with a pint of honeysuckle flower water. This is also good for him to take.[11]

2. Boil kum chow (bark of tree) and wash sore eyes with warm solution.

3. Wash eyes with cold tea.

* As prescribed by Hawaiian Herb Healers of Ancient Hawaii. Excerpts from D. K. Kaaiakamanu.

Filipino

After a baby is born, do not permit his mother to read, nor have a bright light in her room for fear of blindness.[12]

For severe burns of the eyes, irrigate the injured eye with urine.

Japanese

Red birthmarks in infants were believed to be due to the pregnant mother having looked at fire.[13]

For headaches and painful eyes, apply bits of medicated and blessed bits of plaster on forehead. The active ingredients of such plasters include camphor, thymol, methyl salycilic acid, borneol, myrrh, and extract of scopolamine.

The Japanese, Chinese, and Filipinos all believe that if the mother during her pregnancy looks at certain objects the child may be harmed. This symbolism is carried over in most cases to the belief that a child's birthmark or deformity will resemble the object viewed by the mother.

Pterygium

The commonest ocular disease that comes to the attention of the ophthalmologist in Hawaii is pterygium. The disease is not confined to sportsmen, beachboys, plantation employees, fishermen, and those who work out of doors. It is not infrequently noted in children. It sometimes occurs in eyes that were previously diagnosed as having pinguecula. Larsen[14] believes that the frequency of pterygium is due to higher wind velocity and sharper type of dust found in the more recent volcanic areas of Hawaii. Meteorologic factors may also play a role. The cornea has a water content of 80.47 percent. It is possible that evaporation or a biochemical disturbance of its protein or amino-acid content may be factors.

Corboy,[15] among 503 male sugar plantation employees, found pterygium in 87 corresponding to 17 percent. Crawford[16] also reports an over-all incidence of 14 percent. Among military personnel, King[17] found the incidence of pterygium higher in Hawaii than in most sections in the United States. Among 300 patients with pterygium, he noted recurrences in one third.

I agree with Kamel[18] and King that the process begins as a "chronic irritative exposure conjunctivitis." In my experience, there is no universally satisfactory surgical approach for the resection of a pterygium. The technique I've used for the past few years consists of a combination of the Bangerter[19] and the McGavic[20] bare-sclera opperations followed by radiation or beta radiation. High refractive errors, corneal macula, symblepharon, and even blindness may complicate pterygium.

Glaucoma

Glaucoma is uncommon in the islands. Cowan[21] stated that "glaucoma is rarely seen in private practice in Hawaii." The virtual absence of adult primary glaucoma among natives of the Trust Territories of the Pacific was seconded by Crawford.[22] Among 3,845 inhabitants of Koror, Truk, and the Marshall Islands he did not uncover any case of chronic, simple glaucoma. When he did run across tension it was always secondary to local pre-existing eye disease.

According to statistics by the Bureau of Sight Conservation and Work with the Blind, as of June, 1955, there were 62 cases of blindness due to primary adult glaucoma, among 711 patients who were registered as blind in Hawaii. This figure represents less than nine percent of the blind. It is considerably lower than the statistics released by the National Society for the Prevention of Blindness.[23] In 1950 they estimated that 12.8 percent of the blind in the United States were blind because of glaucoma. For a five-year period, from 1949 to 1954, there were 3,867 eye cases admitted to the ophthalmologic services of three of Honolulu's largest civilian general hospitals. Of these, adult primary glaucoma was diagnosed in 179.

According to Fennel[24] "glorious sunshiny weather" has its effects on the psychology of our patient and probably on his physiology as well. As an interesting corollary to this thought are the observations of the medical superintendent of the Territorial Mental Hospital.[25] He noted that major psychotic episodes are fewer, milder, and less violent in Hawaii than in mental hospitals on the mainland.

Infectious diseases

Trachoma

During the past 20 years, active trachoma in clinical practice has been seen only sporadically. From the files of the Bureau of Communicable Diseases of the Territorial Department of Health, for an eight-year period from 1937 to 1944, Enright[26] found 331 cases of active trachoma. Of these 54.7 percent occurred among the Japanese, 4.2 percent among Caucasians. During the past 10 years a further decline was noted. In 1940, Hamman and Holmes[27] found that trachoma ranked third among the causes of blindness in Hawaii. They noted that the disease took its heaviest toll from members of the first generation oriental population. In 1955, as a cause of blindness trachoma slipped from third to fifth place. Dunn[28] in 1931 reported that trachoma per se was not nearly as common as it was then believed. He felt that the disease was commonly mistaken for follicular conjunctivitis which at that time "was practically universal among school children in Hawaii." At the present folliculosis is also on the wane.

Leprosy

During a 10-year period, from 1939 to 1949, Chung Hoon[29] reported 316 new cases of Hansen's disease in Hawaii. 52 percent of these occurred among Hawaiians and part-Hawaiians, 20 percent among Filipinos, 13 percent among Japanese, four percent among the Chinese, four percent among the Portugese, and seven percent among all the other races.

The Territory of Hawaii operates two hospitals for the treatment and care of Hansen's disease patients. One is located at Kalaupapa, Molokai, the other is at Pearl City, Oahu.

Kalaupapa Settlement provides hospital facilities for a present patient load of about 220. These patients are largely those who have had the disease for many years. As a result, they show marked evidences of the disease which include disfiguration, crippling, and often blindness. Although some of the patients have become bacteriologically negative and could be released from the settlement, they choose to continue residence at Kalaupapa due largely to the fact that they have no home, no community to which to return, and also because they require nonancillary care which can only be provided in this understanding community.

Kalaupapa Settlement is laid out on a plan of rural village where about half of the patients live in individual cottages and do their own cooking and housekeeping. The more disabled patients are housed in unit homes with individually furnished room and a community dining room within the area. Many of the patients have married since their admission to the institution. These married couples are assigned individual apartments or houses and plan on continuing residence at Kalupapa for the balance of their lives.

In contrast to the attitude at Kalaupapa, the patients at Hale Mohalu for the most part are eagerly looking forward to the time when they may be released and reunited with their families. This is in part due to the fact that all new patients since 1949 were admitted to Hale Mohalu and have been constantly encouraged to prepare themselves for return to their communities. All patients are required to remain in the division's institutions as long as their tissue scrapings remain bacteriologically positive.

According to an editorial in the March, 1949, issue of the *Annals of Internal Medicine*, a new era has unfolded in the manage-

ment of patients with leprosy:

"The routine isolation of all sufferers is manifestly out of date. At worst, leprosy is less infectious than tuberculosis. Often it is not infectious at all. Elimination of the term leprosy, or leper, is another important step. These words are irretrievably allied with social reproach. 'Living corpses, they wandered to and fro, muffled from head to foot, a hood over the face, and carrying in hand a bell, the Lazarus bell, it was first called, through which they give timely warning of their approach.' (Heine)"

The discovery of sulfone drugs revolutionized the treatment of leprosy and greatly reduced the incidence of ocular complications. Prior to their use, ocular involvement occurred in 90 percent of the lepromatous and mixed groups and in over 50 percent of the tuberculoid form. Prendergast,[30] in 1939, stated that "ocular lesions of leprosy have proved so resistant to treatment that this field has been termed a hopeless branch of ophthalmology."

Madarosis, paralytic lagophthalmos, pannus, superficial punctate keratitis, parenchymatous, discoid and sclerosing keratitis, corneal leproma, anterior and posterior synechias, with seclusio and occlusio pupillæ, and cataracta complicata, and disfiguring anterior staphyloma are still seen among the older patients admitted prior to sulfone therapy. Fortunately the majority of these patients withstand ocular surgery well. The younger patients admitted since the discovery of sulfones are, by and large, relatively free of serious ocular complications.

Epidemic keratoconjunctivitis

In 1941, the first report[31] of an "epidemic keratoconjunctivtis" in the United States came from Hawaii. It was noted that the disease occurred with greatest frequency among employees of the Pearl Harbor Navy Yard. It is well known that by 1942 the disease had spread through the major shipyards of the United States.

Beale's conjunctivitis

A short-lived epidemic of swimming bath conjunctivitis occurred in Honolulu in 1951. According to one estimate it involved approximately one percent of the total island population.

Toxoplasmosis

Stitt and Levine[32] found a striking and significant correlation between physical evidence of chorioretinitis and "dye test" titers for toxoplasmosis in the sera of patients and their mothers whom they studied. The incidence of toxoplasmosis in Hawaii is a matter of conjecture. The prevalence of old, "focal" circumscribed, exudative choroidal lesions and heavily pigmented glial scars of previously undetermined etiology suggests that the disease occurs more frequently than previously suspected.

Industrial hazards

Sugar and pineapple industries

The leaves of sugar cane and pineapple fruit have sawtooth type of thorny edges and taper into sharp pointed ends. While cutting sugar cane, picking or planting pineapple, there is a hazard of direct mechanical injury to the lids, conjunctiva, or cornea. The adoption of an adequate goggle program and the application of fertilizers and other strong chemicals by machines rather

Fig. 1 (Holmes). Both the point and edge of the cane leaf are hazardous. The saw-tooth edge on the cane leaf is primarily responsible for cutting injuries.

than by hand has greatly reduced the incidence of eye injuries on the plantations. In the pineapple industry, during slicing, cutting, and sorting the fruit, pineapple juice frequently gets into the eyes. Due to the relative nonvolatility and low irritability of the chemical components of the pineapple fruit, the juice causes transitory, mild acute conjunctivitis. The chemical composition of the pineapple fruit is as follows:

CHEMICAL COMPOSITION OF THE PINEAPPLE FRUIT

Total sugars	10-16%
Sucrose, $C_{12}H_{22}O_{11}$	7-12%
Reducing sugar, $C_6H_{12}O_6$	3-5%
Acid as citric, (COOH) $CH_2C(OH)$ (COOH) CH_2COOH	0.4-1.3%
pH	3-4
Proterolytic enzyme, bromelain	Present before heating
Carotene pigments	1-2 p.p.m.

TOURIST INDUSTRY

Allergy. In the land of year-round sunshine, tropic trade winds, pleasant balmy weather, modern sanitation, and an alert public health system, there should be little cause for illness or disease. However, the lush, luxuriant, semitropical flora and fauna have been responsible for ophthalmic manifestations of allergy. Keratoconjunctivitis due to crown flower leaves was reported by Wong.[33] This is accompanied by corneal edema, folds in Descemet's membrane, and reflex myopia due to ciliary spasm. The mango, frequently, and the papaya, passion fruit, litchi, pineapple, and guava, occasionally, cause transient edema and hyperemia of the lids and conjunctiva. H. L. Arnold, Jr.,[34] reported dermatitis about the face and eyelids due to Kahili flower. H. L. Arnold[35] summarized and reported the poisonous plants and flowers in Hawaii. He found that several were capable of causing local and systemic disturbances.

The Portuguese-man-of-war, lobster, crayfish, turtle, squid, or octopus are also periodically implicated as etiologic agents responsible for swollen, red eyes.

My introduction, in Hawaii, to the dire sequelae of cosmetics on the eye occurred 18 years ago in a 22-year-old, guitar-strumming, Portuguese-Hawaiian cowboy. This patient developed a corneal ulcer following the application of an "aftershave facial cream" which he purchased from an itinerant vendor. The corneal ulcer went on to purulent panophthalmitis and ended in evisceration. On Waikiki Beach today, several drugstores are advertizing varieties of milk-protein cream, mud-packs, oily pink nail polish, and vitamin complex shampoo for masculine use! For women, according to the beauty column in the local paper, complete eye makeup, eyeshadow, eyebrow pencil, kohl, and mascara have reached such a point of acceptance that even in daylight, "the naked eye is definitely out of fashion!"

In Hawaii, as in all tourist resorts, dermatitis venenata due to cosmetics is of endemic occurrence. Periodic exacerbations occur with the arrival of each ship or plane load of well-groomed male and lovely female visitors.

Vascular or neurovascular accidents. Among the more serious medical and ultimately ophthalmologic complications that befall tourists are those caused by excesses. During a quick trip to Hawaii, several visitors attempt to see everything and do everything. Guests in their fifties and sixties golf, swim, try to learn to ride the surfboard, "catch a wave," row outrigger canoes, and sight-see by the day. In the evening, they eat, drink, and smoke more, dance longer, and stay up later than they are accustomed to doing at home. Pre-existing vascular retinopathies sometimes become aggravated; patients with chronic glaucoma often need increased strengths and dosages of miotic medication during their trip.

CROSSROADS OF THE PACIFIC

Planes and ships to and from the Orient, the Philippines, Australia, New Zealand, the United States, and Canada stop in Hawaii.

So do fishing and sail boats, yachts, and round-the-world pleasure cruisers. Sailors who need a new glass eye, passengers who have broken their glasses, flying personnel whose CAA physical examinations have lapsed demand speedy medical and optical care.

Geographically, Hawaii is also the closest, most up-to-date United States medical center in the Pacific. Patients with serious ophthalmologic problems, cerebral or orbital neoplasms from Wake, Guam and Midway, Samoa, Tahiti, Fiji, and other Pacific Islands sometimes travel to Honolulu for consultation and medical care.

Acts of God and war

Severe postoperative hyphema occurred on the fourth day after cataract extraction following an earthquake; postoperative iris prolapse was noted on April 1, 1947, the day the tidal wave hit the islands. During volcanic eruptions volcanic soot or ash may lodge in the eye. Their clinical course and treatment are no different from that of foreign bodies of nonvolcanic origin.

Trauma

War injuries of the eyes, adnexa, orbits, visual pathways were commonly seen and treated in Hawaii's service hospitals during World War II and the Korean War.

The sale of fireworks is permitted in the Territory of Hawaii. Eye accidents due to explosions of firecrackers occur with great frequency and regularity. Fireworks are especially popular among the oriental population: Chinese-Americans will set them off on all national, Chinese, and Hawaiian holidays, in conjunction with weddings, funerals, or even a dinner party.

Bureau of Sight Conservation

The Bureau of Sight Conservation and Work with Blind was established in 1935 by the territorial legislature. It provides training for the blind in work at the territorial shop for the adult blind, vending stands,

Fig. 2 (Holmes). Blind woman making paper leis.

home industries, and in other employment. The blind who attend these classes make pot holders, rugs, and purses on looper-looms. They learn basketry, crocheting, knitting, ceramics, and loom weaving. The instructor also provides home teaching services to those who are unable to leave their homes. The bureau also provides the blind with red and white canes, whistles, talking book machines, earphones, transportation badges, and radios. Since 1947, an additional service has been offered to the blind in providing tax exemption certificates to those who wish to have such exemptions.

The bureau's work is also concerned with partially seeing persons. In 1938, an annual vision testing program was organized. Over 100,000 students are vision tested annually.

Fig. 3 (Holmes). Flower arrangement class for the blind.

Fig. 4 (Holmes). Blind employees of a Hawaiian pineapple company folding crates.

Fig. 5 (Holmes). Hawaiian, Chinese, and Japanese blind learning to cook.

One out of every 10 children in the territory have been found to need eye care.

Recently two private organizations have begun training seeing-eye dogs for the blind.

Rural eye clinics

On the islands of Molokai and Lanai, housing approximately 4,500 and 2,400 people respectively, there are no ophthalmologists or optometrists. On these islands and in remote rural areas, periodic semi-annual eye clinics sponsored usually by the local Lions Clubs are held.

Medical meetings

The Hawaii Eye, Ear, Nose, and Throat Society, branch of the Hawaii Medical Association, holds regular monthly meetings. It is frequently host to ophthalmologists from the United States and abroad. In glancing at my guest book, the names of Mr. Bertie Nutt, Mr. John Foster, Mr. Seymour Phelps, and Jimmy Doggart from England, Sjøgren from Sweden, Inouye and Sato from Japan, Ida Mann, Bruce Hamilton, A. L. Tostevin, and McAlister Gregg from Australia, and Moacyr Alvaro from Brazil are some of the distinguished foreign ophthalmologists who visited Hawaii during the past five years.

The future of ophthalmology in Hawaii is bright. Perhaps it can be best expressed by the motto in Hawaii's coat of arms:

Ua mau ke ea o ka aina i ka pono.

(The life of the land is perpetuated by righteousness.)

1013 Bishop Street.

References

1. All About Hawaii: Honolulu Star-Bulletin, Honolulu, Hawaii, 80th edition, 1955.
2. Pacific Area Travel Handbook: Menlo Park, Calif., Lane Publishing Company, 1955.
3. Martin, H.: Quoted by Krogman, W. M.: The Anthropology of the Eye. Ciba Symposia, **5**:1607, 1943.
4. Sayoc, B. T.: To be published.
5. Crawford, H. E., and Hamman, G. C.: Racial analysis of ocular defects in the schools of Hawaii. Hawaii M. J., **8**:90, 1949.
6. Rambo, V., Personal communication.
7. Holmes, W. J.: Night vision: I. Comparison of the scotopic visual ratings of young Japanese and Caucasian adults living in Hawaii. Arch. Ophth., **36**:141-154, 1946.
8. Rose, H. W.: Sunglasses. Sight Saving Rev., **25**:100, 1953.
9. Green, L. C., and Beckwith, M. K.: Hawaiian customs and beliefs relating to birth and infancy. Am. Anthropologist, **26**:235, 1924.
10. Handy, E. C. S., Pukui, M. K., and Livermore, K.: Outline of Hawaiian physical characteristics. Bernice P. Bishop Museum Bulletin, **126**:15, 1934.
11. Anon.: Cultural beliefs and practices of the child-bearing period and their implication for nursing practice: I. Chinese beliefs and practices. Hawaii Health Messenger, **16**:2 (Feb.) 1955.

12. ———: Cultural beliefs and practices of the child-bearing period and their implication for nursing practice: II. Filipino beliefs and practices. Hawaii Health Messenger, **16**:3 (Mar.) 1955.
13. ———: Cultural beliefs and practices of the child-bearing period and their implication for nursing practice: III. Japanese traditions and customs. Hawaii Health Messenger, **16**:4 (Apr.) 1955.
14. Larsen, N. P.: Personal communication.
15. Corboy, P. M.; An EENT examination of plantation workers. Plantation Health, **9**:3 (July) 1941.
16. Crawford, H. E.: The Kohala Eye, Ear, Nose, and Throat Clinic. Tr. 1st ann. meet. Territorial A. Plantation Physicians of Hawaii, 1944, p. 78.
17. King, J. H., Jr.: The pterygium: Brief review and evaluation of certain methods of treatment. Arch. Ophth., **44**:854 (Dec.) 1950.
18. Kamel, S.: Pterygium: Its nature and a new line of treatment. Brit. J. Ophth., **30**:549 (Sept.) 1946.
19. Bangerter, A.: Pterygium operation and covering of conjunctival defects. Ophthalmologica, **106**: 316 (Dec.) 1953.
20. McGavic, J. S.: Surgical treatment of recurrent pterygium. Arch. Ophth., **42**:726 (Dec.) 1949.
21. Cowan, T. W.: Report of mainland trip. Straub Clinic Proc., **21**:53-57, 1955.
22. Crawford, H. E., Hamman, G. C., and Lanwi, I.: Ophthalmological survey of the trust territories of the Pacific Islands. Publ. Trust Terr. of the Pacific.
23. Changing problem in prevention of blindness, U.S.A. 1940-1950. Bull. Natl. Soc. Prevent. Blindness, New York, 1951.
24. Fennel, E. A.: Discussion of paper by Bowles, H. E.: Eclampsia and the weather in Hawaii. Hawaii M. J., **8**:194 (Jan.) 1949.
25. Kimmich, R.: Personal communication.
26. Enright, J.: Personal communication.
27. Holmes, W. J., and Hamman, G. C.: Causes of blindness in Hawaii. Arch. Ophth., **25**:643-650, 1941.
28. Dunn, W. T.: Trachoma. Tr. M. Soc. Hawaii, 1931, p. 35.
29. Chung Hoon, E. H.: Hansen's disease in Hawaii, 1939-1949. Hawaii M. J., **1**:305-309, 1950.
30. Prendergast: Quoted by Holmes, W. J.: Changing concepts of ocular leprosy. Tr. Pacific Coast Oto-Ophth. Soc., 1954, pp. 51-56.
31. Holmes, W. J.: Epidemic infectious conjunctivitis. Hawaii M. J., **1**:11 (Nov.) 1941.
32. Stitt, G. B., and Levine, M.: The possible existence of clinical toxoplasmosis in Hawaii. Hawaii M. J., **12**:351 (June) 1953.
33. Wong, W. W.: Keratoconjunctivitis due to crownflower. Hawaii M. J., **8**:337, 1949.
34. Arnold, H. L., Jr.: Kahili flower (Grevillea banksii) dermatitis. Hawaii M. J., **1**:15, 1941.
35. Arnold, H. L.: Poisonous plants of Hawaii. Honolulu, Tongg Publishing Co., 1944.

THE SCLERAL INSERT (SCLEROCLEISIS) FOR GLAUCOMA*

A PRELIMINARY REPORT OF THREE CASES

A. B. VICENCIO, M.D.
Cebu City, The Philippines

The varied operations for glaucoma, as those for pterygium, attest that the ideal surgical procedure for this dreaded disease is not yet at hand.

This preliminary report of three cases is experimental in nature. The paramount aim was to avoid evisceration or enucleation in absolute glaucoma, which, psychologically, our people are loath to undergo. Besides, the expense of an implant, whose permanent retention in the orbit is still uncertain, and the cost of the prosthesis, with its daily care, is beyond the reach of most patients. Cosmetic retention of the eyeball and relief of the nagging headache were, therefore, the main purposes of this experiment.

After a cyclodialysis, Bietti[1] used a polyethylene tube insert, while Troncoso[2] used magnesium wire. Muldoon[3] and Bick[4] employed tantalum-wire setons, and Bock,[5] Jena or Pyrex glass setons. During the XVII International Congress of Ophthalmology,

* From the Eduarda Bautista Research for Eye, Ear, Nose, and Throat.

absorbable pliofilm was shown as an insert. All these inserts and setons are intended to facilitate the outflow of aqueous humor from the anterior chamber to the newly formed channel, thereby reducing the intraocular pressure.

The procedures just mentioned have not come into popular use because, like corneal contact lenses and the Ridley plastic implant after cataract extraction, the inserts and setons act as foreign bodies whose tolerance by the eye is questionable.

To test the scleral insert for foreign-body irritation in the anterior chamber, four cats' eyes were studied before the procedure was used on human eyes. Clinically (one week to two months), there were absolutely no signs of inflammatory reaction in the cats' eyes. Unfortunately, no facilities for histologic study of the cats' eyes were available in Cebu City.

Iris-inclusion operations, such as iridenclesis or iridotasis, have lately almost supplanted the Elliott trephination and allied procedures in treating glaucoma. The iris, as an integral part of the eye, avoided the foreign-body reaction and proved to be very effective in the control of tension in early cases of glaucoma.

In absolute glaucoma, however, where rather than restoration of vision the main concerns are conservation of the eyeball, lowering of the intraocular pressure, and abolishing the persistent headache, iridencleisis usually fails. Resort to cyclodialysis with its modifications or to cyclodiathermy or to cycloelectrolysis becomes the choice short of evisceration or enucleation. Even then, the results are uncertain, eventually leading to removal of the eye.

The scleral insert or, to venture on a new terminology, "sclerocleisis," follows the principle of iridencleisis and is similar to the techniques employing inserts and setons, by which a filtering channel is obtained between the anterior chamber and the subconjunctival space.

Technique

A limbus-based conjunctival flap is incised, dissected, and folded over the cornea below, as for iridencleisis. A half-thickness lamellar scleral strip about three-mm. wide and six-mm. long (giving allowance for shrinkage) is dissected by a No. 15 Bard-Parker knife from above downward, the base of the scleral flap being attached to the limbus. Just anterior to the base of the strip of sclera (one to two mm. is the best), a keratome incision is made at the limbus, three to four mm. long, and into the anterior chamber. With fine forceps, the very soft and pliable scleral strip is easily inserted between the sclerocorneal incision into the anterior chamber. The conjunctival flap is closed with continuous silk sutures.

Compared to iridencleisis, the scleral insert is a little harder to prepare. Especially bothersome is the bleeding from the deep scleral vessels, always obscuring the field of incision. Cauterization controls the hemorrhage easily but it is avoided so as not to char the insert. With practice, a scleral insert could be dissected within five minutes.

In as much as the sclera is also an integral part of the eye, like the iris, the only basic difference between iridencleisis and sclerocleisis is that, in the former procedure, the iris is pulled out of the anterior chamber and, in the latter, the scleral strip is pushed into the anterior chamber.

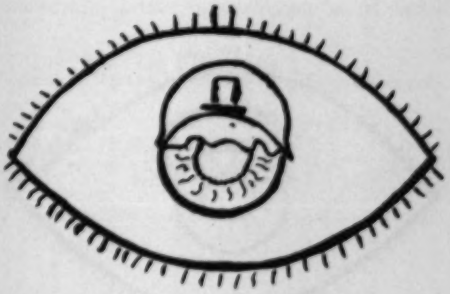


Fig. 1 (Vicencio). Scleral strip dissected and keratome incision at limbus.

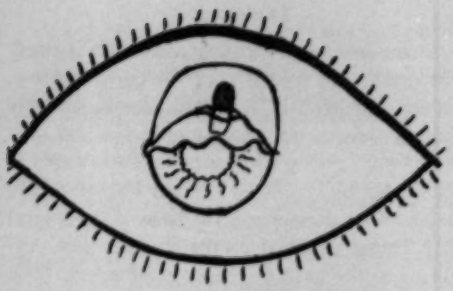


Fig. 2 (Vicencio). Scleral strip inserted into anterior chamber through keratome incision.

Case reports

Case 1

Mrs. L. A., aged 62 years, complained of redness of the right eye and headache of the right side since April, 1955. She was first seen in the office on November 25, 1955, eight months later.

Vision was: O.D., blind; O.S., 20/70, J8 (no correction).

Tension was: O.D., 90 mm. Hg (Schiøtz) with a 10 gm. weight; O.S., 22 mm. Hg, with a 5.0-gm. weight.

Diagnosis: glaucoma, absolute, right eye, with a mature cataract. She refused evisceration or enucleation. Due to the persistent headache, however, she came back and consented to sclerocleisis on December 9, 1955.

The first postoperative tension was taken December 15, 1955: O.D., 42 mm. Hg with 10-gm. weight. The tension remained 42 mm. Hg until December 26th, when she went home to a neighboring island. Curiously

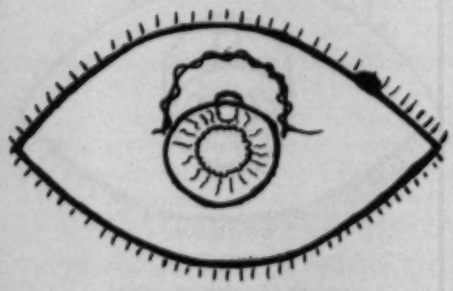


Fig. 3 (Vicencio). Conjunctival flap sutured and scleral insert in place.

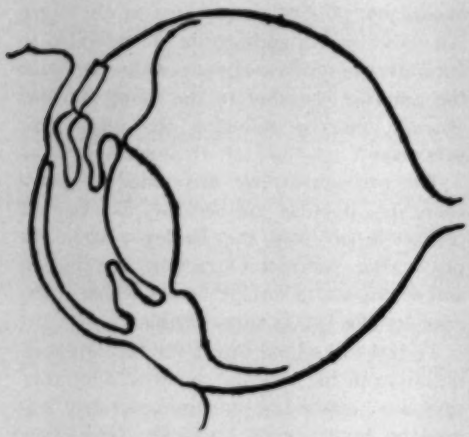


Fig. 4 (Vicencio). Scleral strip in anterior chamber.

enough, even if the tension did not go down to normal, the headache became very slight, the patient was comfortable, and the eye started to get white.

Comment. This case illustrates the feasibility of retaining the eyeball in absolute glaucoma. She was the first patient experimented on. She had no more vision to lose in the right eye and good vision in the left eye. Hence, if the procedure failed, no uneasy conscience would hound me at night.

Case 2

Mrs. E. B., aged 30 years, was first seen on December 8, 1955, with a large uveal mass at the upper limbus of the left eye.

Vision was: O.D., blind; O.S., poor light perception.

Tension was: O.D., 45 mm. Hg (Schiøtz) with a 5.0-gm. weight; O. S., hypotensive. On August 26, 1955, the left eye was struck by a piece of stick which apparently penetrated the upper limbus, with prolapse of the iris. Gradually the sight of the right eye disappeared.

Diagnosis: Cyst, extraocular, iris, left eye. Sympathetic ophthalmia, right eye, with optic atrophy and secondary glaucoma. On December 12, 1955, the iris cyst of the left eye was excised. The wound was closed with

corneoscleral sutures and covered with a conjunctival flap. Sclerocleisis of the right eye, was done at the same sitting. Tension of right eye on December 26th was, 25 mm. Hg (Schiøtz) with a 5.0-gm. weight. There was no more headache. Vision was: O.D., blind; O.S., hand movements at one foot.

Comment. This was another case of a hopeless eye where trial of sclerocleisis would do no harm to the patient and do the science of ophthalmology some good.

Case 3

Mrs. T. M., aged 50 years, was first seen on December 14, 1955, complaining of redness of both eyes, severe headache, and blindness since November, 1955.

Vision was: O.D., doubtful light perception; O.S., poor light perception.

Tension was: O.U., 90 mm. Hg (Schiøtz) with a 10-gm. weight.

Diagnosis. O.D., absolute glaucoma; O.S., almost absolute glaucoma. Bilateral sclerocleisis was done on December 17, 1955. The last tension was taken on December 26th: O.D., still remained 90 mm. Hg, with vision of hand movements at one-half foot; O.S., 22 mm. Hg with a 5.0-gm. weight, and vision of 10/200.

Comment. In nine days, sclerocleisis failed to lessen the tension of the right eye but the vision improved somewhat, while the tension of the left eye went down to normal, also with improvement of vision so that the patient could walk by herself. Again, in spite of the high tension of the right eye there was very little headache on the same side, which I could not explain. This patient gained something out of nothing. This case also altered my original aim of preserving only the eyeball, as it seems that sclerocleisis will work in early cases of glaucoma.

Discussion

These three cases are a very small series to start with but I think they are enough to present the procedure. Follow-up of these three pioneer cases, plus additional new cases in the future, with, perhaps, some modifications, such as making the scleral flap wider, may improve this maiden effort in sclerocleisis. If this procedure proves to be worthy, it will obviate such objectionable features of iridencleisis as a distorted pupil, and the hyphema secondary to cutting the iris, especially in rubeosis iridis. Sympathetic ophthalmitis, although not very frequent, is a hazard which this procedure eliminates. And there is no danger of injuring the lens.

Summary and Conclusion

Three cases of glaucoma in which a scleral insert or sclerocleisis was done are reported. The results appear to be promising. These cases are reported so that other investigators may try this new technique and improve it with their own modifications.

581 Jones Avenue.

References

1. Bietti, G. B.: Plastic drainage in cyclodialysis. Ateneo parmense, **23**:8, 1952.
2. Troncoso, M. U.: Cyclodialysis with insertion of metal implant in treatment of glaucoma: A preliminary report. Arch. Ophth., **23**:270 (Feb.) 1940.
3. Muldoon, E. W., et al.: Platinum implant in glaucoma surgery. Arch. Ophth., **45**:666 (June) 1951.
4. Bick, M.: Use of tantalum for ocular drainage. Arch. Ophth., **42**:373 (Oct.) 1949.
5. Bock, R. H.: Subconjunctival drainage of the anterior chamber by a glass seton. Am. J. Ophth., **33**:929, 1950.

THE ALTERATIONS IN AQUEOUS-HUMOR LACTATE CONCENTRATION*

Following systemic carbonic anhydrase inhibition

Bernard Becker, M.D., and Marguerite A. Constant, Ph.D.
Saint Louis, Missouri

The concentration of lactate in the aqueous humor of the anterior and posterior chambers of the rabbit eye has been found to be considerably in excess of the plasma concentration.[1] It has been assumed that this excess of lactate in the ocular fluids results from its local accumulation as a product of the glycolytic metabolism of such intraocular structures as the lens and cornea. The concentrations reported represent the resultant excess in spite of the loss of lactate from the anterior chamber by both diffusion and outflow. If these assumptions are correct, then any decrease in rate of aqueous flow should result in a greater accumulation of lactate in the eye. In other words, a relatively more stagnant aqueous should have a greater lactate excess as compared with plasma concentrations. Previous investigations have indicated that the systemic administration of a carbonic anhydrase inhibitor results in approximately 60-percent suppression of aqueous flow in rabbit eyes.[2-4] In the present study the effects of acetazoleamide† upon the concentrations of lactate in the posterior chamber, anterior chamber, and plasma of rabbits were determined.

Methods

Male albino rabbits, weighing two to three kg. (Haskins Rabbitry, Saint Louis), were used. Blood was obtained by cardiac puncture into heparinized syringes. It was centrifuged at once in the cold and the plasma was separated from red cells as rapidly as possible. Posterior chamber and anterior chamber fluid samples were obtained from the tetracaine-anesthetized, proptosed eye into calibrated pipets.

Acetazoleamide was administered as the sodium salt in doses of 100 mg./kg. intravenously followed by 25 mg./kg. intraperitoneally every 30 minutes. Each animal had the initial blood and aqueous samples drawn from one eye before acetazoleamide administration.

Lactate was determined by the method of Barker and Summerson[5] as modified by Kinsey.[1] The second blood and samples from the other eye were obtained after 20 minutes or six hours of carbonic anhydrase inhibition. Blood samples were always drawn before eye samples to minimize the effect of excitement on plasma lactate concentrations. Each animal eye was punctured on only one occasion and then the animal was discarded.

Results

Steady-state concentrations of lactate in the posterior and anterior chambers were found to be in excess of the plasma concentrations by an average of 5.4 ± 1.2 mM/L and 3.9 ± 1.0 mM/L respectively in the 24 rabbits of this experiment (tables 1 and 2—Before acetazoleamide).

Following six hours of acetazoleamide administration to 13 rabbits, the posterior chamber and anterior chamber concentrations of lactate were found to rise in spite of a falling plasma lactate level (table 1). A new steady-state was thus approached in which the posterior chamber concentration of lactate rose to an average excess over plasma of 8.1 ± 1.4 mM/L; anterior chamber concentrations also rose significantly

* From the Department of Ophthalmology, Washington University School of Medicine, and the Oscar Johnson Institute. This investigation was supported in part by a research grant, B-621, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service.

† Acetazoleamide (Diamox) used in this study was supplied through the courtesy of Dr. James D. Gallagher, Clinical Research Section, Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

TABLE 1

LACTATE CONCENTRATION (MM/L)

	Before Acetazoleamide					Six Hours after Acetazoleamide				
	C_{PI}	C_{PC}	C_{PC}-C_{PI}	C_{AC}	C_{AC}-C_{PI}	C_{PI}	C_{PC}	C_{PC}-C_{PI}	C_{AC}	C_{AC}-C_{PI}
	2.0	7.2	5.2	6.9	4.9	1.3	8.0	6.7	7.0	5.7
	1.5	7.2	5.7	6.7	5.2	1.1	8.8	7.7	6.8	5.7
	1.6	9.2	7.6	7.8	6.2	1.6	10.9	9.3	9.3	7.7
	2.0	6.3	4.3	5.3	3.3	1.1	8.3	7.2	6.3	5.2
	4.4	9.9	5.5	6.9	2.5	1.7	13.1	11.4	8.7	7.0
	6.4	8.8	2.4	8.5	2.1	0.9	9.1	8.2	8.3	7.4
	2.6	7.4	4.8	7.4	4.8	1.2	7.8	6.6	7.0	5.8
	1.8	—	—	5.8	4.0	0.7	7.3	6.6	6.9	6.2
	2.1	7.3	5.2	5.9	3.7	1.1	7.9	6.8	6.2	5.1
	2.9	10.9	8.0	7.0	4.1	1.4	8.2	6.8	7.2	5.8
	2.5	8.8	6.3	6.8	4.3	1.0	10.7	9.7	7.0	6.0
	2.7	7.8	5.1	7.1	4.4	2.3	11.3	9.0	8.2	5.9
	3.2	9.1	5.9	5.8	2.6	1.6	10.5	8.9	8.1	6.5
Mean	2.7	8.3	5.5	6.8	4.0	1.3	9.4	8.1	7.5	6.2
S.D.			±1.4		±1.1			±1.4		±0.8

to a mean of 6.2 ± 0.8 mM/L greater than the plasma concentration.

Since the falling plasma tended to offset in part the rise in aqueous lactate, short-term experiments were carried out on 11 rabbits (table 2). After 20 minutes of carbonic-anhydrase inhibition, there was no significant change in the concentration of lactate in the plasma but a most significant rise in the posterior chamber aqueous from an average initial concentration of 9.8 mM/L to a level averaging 13.0 mM/L. The aqueous of the larger anterior chamber had risen less dramatically in this short time interval. Thus, the posterior chamber excess over plasma increased from a mean of 5.3 ± 0.9 to 8.6 ± 1.4, whereas, the anterior chamber excess changed from 3.8 ± 0.9 to 4.9 ± 0.7 mM/L.

DISCUSSION

The results recorded confirm the excess of lactate in the anterior chamber fluid of the rabbit eye and an even greater excess in the posterior chamber fluid.

One simple assumption is that part of the lactate enters the normal eye with the secreted aqueous at plasma concentrations (3.6 mM/L) and that the remainder (5.4

TABLE 2

LACTATE CONCENTRATIONS (MM/L)

	Before Acetazoleamide					Twenty Minutes after Acetazoleamide				
	C_{PI}	C_{PC}	C_{PC}-C_{PI}	C_{AC}	C_{AC}-C_{PI}	C_{PI}	C_{PC}	C_{PC}-C_{PI}	C_{AC}	C_{AC}-C_{PI}
	5.4	11.1	5.7	8.8	3.4	5.8	13.2	7.4	9.9	4.1
	3.3	9.1	5.8	8.3	5.0	4.2	13.3	9.1	8.8	4.6
	3.6	10.0	6.4	8.8	5.2	5.5	15.1	9.6	10.1	4.6
	2.0	8.7	6.7	6.8	4.8	1.1	10.5	9.4	6.6	5.5
	2.4	7.2	4.8	6.0	3.6	2.2	11.5	9.3	6.8	4.6
	3.2	7.0	3.8	6.2	3.0	2.7	13.6	10.9	6.7	4.0
	3.3	9.4	6.1	8.0	4.7	4.1	14.0	9.9	8.5	4.4
	6.9	12.3	5.4	9.8	2.9	7.9	16.0	8.1	12.1	4.2
	6.5	10.4	3.9	9.7	3.2	4.0	11.3	7.3	9.9	5.9
	6.6	11.7	5.1	9.2	2.6	5.7	12.4	6.7	11.4	5.7
	6.2	10.8	4.6	9.8	3.6	4.9	11.9	7.0	10.7	5.8
Mean	4.5	9.8	5.3	8.3	3.8	4.4	13.0	8.6	9.2	4.9
S.D.			±0.9		±0.9			±1.4		±0.7

mM/L) of the posterior chamber concentration is produced locally. Since aqueous is secreted in the normal rabbit eye at approximately 3.0 to 3.5 cu. mm./min., this would require local production into the posterior chamber of at least 0.016 to 0.019 μM/min., or about 1.0 to 1.2 μM/hr. (assuming no diffusional losses). Merriam and Kinsey[6] have estimated the production of lactate by the rabbit lens from in vitro culture experiments at 1.0 to 1.5 μM/hr. Thus, the lens is capable of supplying all of the lactate excess found in the posterior chamber aqueous.

Although acetazoleamide administration increases the excess lactate in the posterior chamber to 8.1 mM/L, this is not comparable to the 60 to 65-percent decrease in rate of aqueous flow induced. Following acetazoleamide, the local production into the posterior chamber may be estimated at 0.008 to 0.010 μM/min., or approximately 0.5 to 0.6 μM/hr. Thus, carbonic anhydrase inhibition appears to decrease lactate production into the posterior chamber by some 50 percent. It is of considerable interest in this regard that there is the same order (50 percent) decrease in plasma lactate following prolonged carbonic anhydrase inhibition (table 1). This finding remains unexplained, but suggests a generalized metabolic effect of acetazoleamide upon lactate production or utilization in the rabbit. More data are needed to evaluate the effects of acetazoleamide on glycolysis in such structures as the lens, as well as in other rabbit organs.

The situation in the anterior chamber is probably much more complex. Here, there is loss of lactate by bulk outflow and diffusion from aqueous to plasma. In addition to entry from the posterior chamber, however, there is likely to be local production into the anterior chamber from lens, cornea, and other structures. The present data are inadequate to differentiate alterations in the rate of diffusion of lactate or its local production into the anterior chamber following acetazoleamide administration.

Summary

In rabbit eyes six hours of systemic carbonic anhydrase inhibition by acetazoleamide resulted in significant increases in the aqueous humor excess over plasma concentration of lactate. The posterior chamber aqueous lactate rose from an excess of 5.4 ± 1.2 mM/L to 8.1 ± 1.4 mM/L and the anterior chamber aqueous increased from 3.9 ± 1.0 mM/L to 6.2 ± 0.8 mM/L as compared with plasma levels. The rise in lactate in the posterior chamber was completed in the first 20 minutes following acetazoleamide, whereas, the anterior chamber aqueous concentration was altered more slowly.

640 South Kingshighway (10).

References

1. Kinsey, V. E.: Comparative chemistry of aqueous humor in posterior and anterior chambers of rabbit eye: Its physiologic significance. Arch. Ophth., **50**:401, 1953.

2. Becker, B., and Constant, M. A.: Experimental tonography: The effect of the carbonic anhydrase inhibitor, acetazoleamide, on aqueous flow. Arch. Ophth., **54**:321, 1955.

3. Becker, B.: The effects of the carbonic anhydrase inhibitor, acetazoleamide, on the composition of the aqueous humor. Am. J. Ophth., **40**:129 (Pt II) 1955.

4. ———: The effects on acetazoleamide on ascorbic acid turnover: An application of the theory of aqueous humor dynamics. Am. J. Ophth., **41**:522-529 (Mar.) 1956.

5. Barker, S. B., and Summerson, W. H.: Colorimetric determination of lactic acid in biological material. J. Biol. Chem., **138**:535, 1941.

6. Merriam, F. C., and Kinsey, V. E.: Studies on the crystalline lens: Technic for in vitro culture of crystalline lens and observations on metabolism of the lens. Arch. Ophth., **43**:979, 1950.

TECHNIQUE OF BIOMICROSCOPY OF THE POSTERIOR EYE*

HANS ROTTER, M.D.
Vienna, Austria

There are two main reasons for reviewing this subject.

The study of the posterior segment of the eye as described in Hruby's book *Spaltlampenmikroskopie des hinteren Augenabschnittes* is of similar significance as Vogt's first *Atlas* on the anterior segment of the eye. But in spite of the importance of the biomicroscopy of the posterior eye English-speaking ophthalmologists still lack an adequate explanation of the technique.

On the other hand, most of the manufacturers of slitlamps have become aware of the advantages in providing additional equipment for biomicroscopy of the posterior eye. Unfortunately, this supplementary equipment on some slitlamps has apparently been planned and constructed without consulting experts on this subject and without showing the necessary appreciation for it. By neglecting indispensable principles, construction inadequacies are followed by unsatisfactory results that hinder the propagation and development of the method. Nevertheless, there are two modern slitlamps excellent for biomicroscopy of the posterior eye—the slitlamp of Haag-Streit and the slitlamp of Carl Zeiss. I shall deal mainly with these two slitlamps when discussing the technique of biomicroscopy of the posterior eye.

Once again, it should be emphasized that the aim of any biomicroscopy must be the stereoscopic observation of the eye in the optical section achieved by obliquely incident illumination. Practical experience shows this to be true with the anterior eye as well as the posterior eye where this examination is always superior to any kind of monocular or binocular observation in diffuse illumination, or even in central slitillumination, and, therefore, should be attempted in every case.

The principal purpose of this paper is to discuss the problems of the technique of biomicroscopy of the posterior eye. This section will be followed by another one summarizing the instructions as to the technique, and, finally, the constructive details indispensable to a successful technique will be presented.

I. PROBLEMS INVOLVING THE TECHNIQUE OF BIOMICROSCOPY OF POSTERIOR EYE

The technical difficulties of the biomicroscopy of the posterior eye are due to two main problems: (1) The necessity of a preset lens or a contact glass and (2) to the diaphragming action of the iris.

A. PRESET LENS OR A CONTACT GLASS

A corneal microscope is capable of providing a focused image of any point within the anterior eye but it cannot image the fundus located at infinity (case of an emmetropic eye) without the aid of additional optical equipment.

As one may conclude, a contact glass (fig. 1-a) with an approximately plain anterior surface can almost nullify the refractive power of the corneal surface and make the fundus accessible to microscopic observation and slitillumination. Moreover, a powerful concave or convex lens (fig. 1-b and c) can change the corneal microscope into a telescope capable of imaging the fundus.

Our experience has led us to believe that a concave preset lens is well suited for general clinical application. It is much easier to handle than the contact glass. When observing the fundus of a highly myopic eye, a convex preset lens should be used. To obtain a clear image of certain peripheral parts

* From the Second Eye Clinic of the University of Vienna, Temporary Director, Doz. Karl Hruby. I wish to express my gratitude to Vernon F. Lightfoot, Logan, Utah, for his assistance in writing this paper.

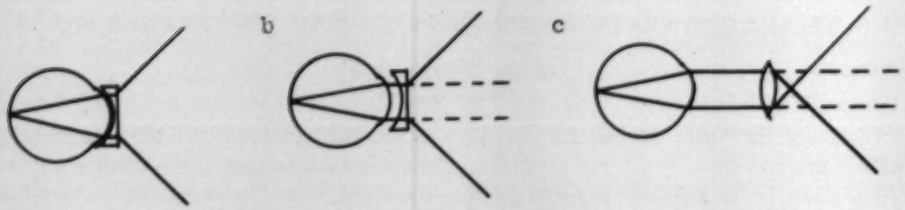


Fig. 1 (Rotter). Schemed paths of rays when using a contact glass (a), a concave preset lens (b), a convex preset lens (c).

of the fundus the contact glass with three mirrors (Goldmann) can be used.

B. Diaphragming action of iris

When observing binocularly the iris acts as diaphragm, so that the two monocular fields are displaced crosswise. The central almond-shaped part belonging to both of the monocular fields is the stereoscopic field. With the illumination being incident from the right side the image of the slit is located within the left half of the stereoscopic field (concave preset lens, contact glass) and appears to be shorter in the field of the left eye of the observer than in the field of the right eye (fig. 2).

The size of the stereoscopic field, and the question as to whether the image of the slit is located within the stereoscopic field, are due mainly to the size of the angle of convergence of the microscopic objectives and to the size of the angle of incidence of the illumination.

The quality of stereoscopic observation improves by increasing the angle of convergence of the microscopic objectives (Ψ, fig. 3-a). This angle is bisected by the main visual line.

The resolving power of the image as to depth improves by increasing the angle of incidence of the illumination upon the main visual line (δ, fig. 3-b). The central slitillumination provides the least useful optical section. Supposing the angle of incidence (δ) being constant the most favorable opti-

TABLE 1

Advantages and disadvantages of the concave preset lens, the contact glass, and the convex preset lens

	Concave Preset Lens (Hruby)	Contact Glass with Three Mirrors (Goldmann)	Convex Preset Lens (El Bayadi)
Mode of Examination	Easy	Rather difficult	Easy
Qualification for general clinical application	Perfect	Limited	Perfect
Examination of the moving eye	Easy	Almost impossible	Easy
Stereoscopic accessibility of the hypermetropic fundus and of the vitreous cavity	Excellent	Good	Moderately good
Stereoscopic accessibility of the myopic fundus	Very poor	Poor	Moderately poor
Field being viewed simultaneously	Small	Moderately large	Large
Surface reflections	Numerous	Few	Numerous
Periphery of the fundus	Distorted visible	Clearly visible, but only above and below in the optical section	Distorted visible
Image	Erect	Erect in the center reflected by the mirrors	Inverse

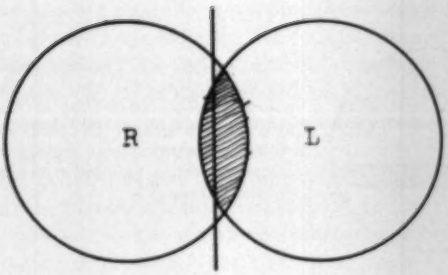


Fig. 2 (Rotter). The stereoscopic field.

cal section is located perpendicular to the plane of both sides of the angle δ.

The total angle between the axis of illumination, and the axis of the microscopic objective farther away from the light, is $\Psi/2 + \delta$ (fig. 3-c).

The stereoscopic accessibility of the fundus results from the location of the slit image within the stereoscopic field, or—in other words—from the angle $\Psi/2 + \delta$ intersecting the pupil as a whole. Either side of this angle may be cut off by the edge of the pupil: either the axis of illumination is not allowed to pass the pupil, resulting in loss of the illumination completely, or the axis of the objective farther away from the light strikes the iris and is followed by loss of stereoscopic observation.

Therefore, the vignetting effect of the pupil calls for a small angle $\Psi/2 + \delta$. This can be achieved by providing a small angle of convergence of the microscopic objectives and a small angle of incidence of the illumination upon the main visual line.

This statement is contradictory to the above mentioned need for a large angle of convergence and for a large angle of incidence. So we have to make a compromise. It has proved to be more advantageous to maintain stereoscopic observation even with a small angle of convergence of the microscopic objectives than to change over to monocular observation. Besides, the smallest angle of incidence resulting from the lamp arm and the microscope arm being approximated precisely is always superior to central illumination and should be preferred for this reason.

On the other hand, while examining parts of the eye that are located not so deeply, as for example, the vitreous cavity or the fundus of an aphakic eye, the resolving power of the image as to depth can and should be improved by increasing the angle of incidence. Of course, this manipulation is limited by the horizontal diameter of the pupil that ought to be extremely dilated for this reason.

The usual lateral position of the lamp arm causes the image of the illuminating slit to be located to one side of the two images of the microscopic objectives. Thus, the pupillary area serving these three paths of rays intersecting in a linear fashion is situated predominantly within the horizontal diameter of the pupil (fig. 4-a). However, the application of the horizontal optical section, with the illumination being incident from above or from below, images the illuminating slit at the pupillary entrance of the patient's eye horizontally above or below the two images of the microscopic objectives (fig. 4-b). Thus the pupillary area serving these three intersecting paths of rays makes better use of the circular shape of the normal pupil than with the usual observation in the sagittal optical section. It is obvious that in cases of pupils that cannot be dilated to the utmost the stereoscopic accessibility of the fundus can be obtained with the observation in the horizontal optical section rather than with the observation in the sagittal one. Also, the horizontal optical section facilitates the stereoscopic accessibility of the lateral periphery of the fundus.

II. Instructions for Technique of Biomicroscopy of Posterior Eye

A. Preparation of Patient

Extreme mydriasis has to be forced by means of a cycloplegic, for example, 0.25-percent scopolamine. Mydriasis resulting from sympathicomimetics is usually insuf-

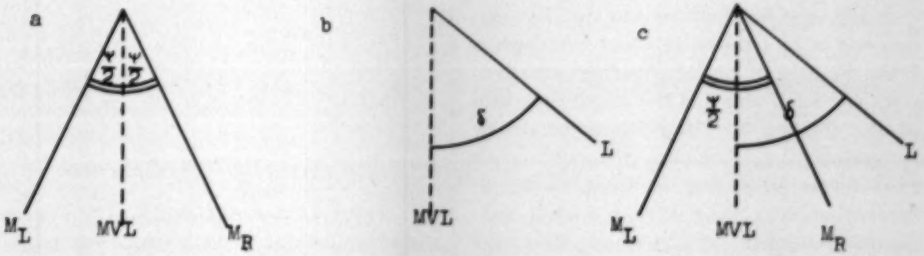


Fig. 3 (Rotter). (a-c). The angle of convergence (ψ) of the microscopic objectives (M_L and M_R) and the angle of incidence (δ) of the illumination (L) upon the main visual line (MVL).

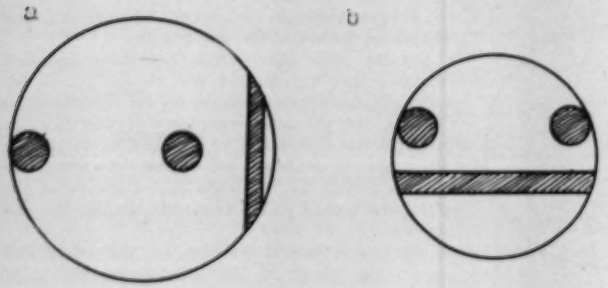


Fig. 4 (Rotter). The images of the illuminating slit and of the two microscopic objectives at the pupillary entrance of the patient's eye when observing with the sagittal optical section (a) and with the horizontal one (b).

ficient since the bright illumination causes some reaction of the pupil.

B. Preparation of slitlamp

1. The *fixation lamp* should be followed by the patient's eye that is not under examination. It makes possible:

a. To look for certain areas of the fundus and to maintain the desired spot in the center of the field.

b. To look over objects of large extent, for example, the vitreous cavity.

c. To lead the rotations of the globe when observing the moving eye.

2. *The lamp arm* has to be brought into a position that allows the illumination to be incident from the temporal side. Otherwise, the illuminating lens or the reversing prism of the slitlamp of Carl Zeiss would collide with the fixation lamp. When using the slitlamp of Haag-Streit the lamp arm located nasally cannot be moved toward the patient since it would strike the holder of the preset lens that is situated in front of the patient's nose.

3. *The angle of incidence* of the illumination has to be reduced to about five degrees from the axis of the neighboring objective:

a. The lamp arm and the microscope arm of the slitlamp of Haag-Streit are closely approximated and the angle reduction prism (Goldmann) is swung in front of the illuminating lens. Since there is a small elongation of the paths of rays when passing the angle reduction prism (Goldmann), the image of the slit has to be refocused.

b. The lamp arm of the slitlamp of Carl Zeiss is brought 10 degrees from the main visual line.

4. The *preset lens* is swung in front of the eye to be examined.

a. When using the slitlamp of Haag-Streit, the preset lens is to be centered on the axis of the patient's eye. The concave lens is brought very close to the patient's cornea. The distance of the convex lens from the corneal surface should be about 17 mm., that is, the focal distance of the lens. The preset lens once being located properly in front of the patient's eye does not have to be moved during the examination itself; all that has to be done is an occasional slight correction of its position.

b. The preset lens of the slitlamp of Carl Zeiss is automatically centered to the corneal microscope; the corneal distance is maintained constantly during the same examination by means of a "fender," but cannot be adapted to individual needs.

5. A *×10 to ×12 magnification* by the corneal microscope is recommended for examining systematically areas of large extent, because of offering a larger depth of focus than that of higher magnifications. The latter should be applied after having found the desired spot.

C. Examination of posterior eye

1. *The typical manipulation.* The systematic examination of the vitreous cavity and the fundus itself calls for mainly sagittal movements of the coupled system of corneal

microscope and illumination. These movements are done while the eye does not change its position. On the other hand, the examination of predominantly frontal planes requires movements of the observed eye associated with slight frontal movements of the coupled system according to the position of the pupil of the observed eye.

As a rule, the actual movements are combinations of both. However, both kinds of movements need the same manipulation, namely, to direct the patient's eye indirectly by means of the fixation lamp with one hand, and to perform well-balanced movements of the coupled system of corneal microscope and illumination with the other hand. This has to be done in such a way that the axis of illumination intersects the pupil as close as possible to its temporal edge (in the case of the concave lens). Otherwise, stereoscopic observation would be lost, since the axis of the objective farther away from the light would not be able to pass the pupil. This manipulation keeps both hands busy; there is no need for moving the preset lens during all the time of examination.

2. *Occasional manipulations.*

a. Once in a while the image of the slit has to be refocused. This can be done when using the slitlamp of Haag-Streit but, unfortunately, not when using the slitlamp of Carl Zeiss.

b. To swing around the coupled system of corneal microscope and illumination permits escape of the disturbing reflections and is an indispensable aid in examining one-eyed patients whose eyes cannot be directed with the fixation lamp. Goldmann has recommended this maneuver for those cases in which the desired spot is already seen monocularly and stereoscopic observation is to be obtained.

c. A temporary enlargement of the angle of incidence of the illumination upon the main visual line offers more useful conditions for stereoscopic observation in the anterior and central part of the vitreous cavity and in the fundus of aphakic eyes.

d. After having found the desired spot a higher magnification can be used to increase the resolving power of the image.

e. Decentering the preset lens allows further observation of the periphery of the fundus. Decentering has to be done in the direction opposite to the direction of gaze of the observed eye when using a concave lens but in the same direction when using a convex lens.

f. There is some difficulty when investigating the lower half of the fundus or of the vitreous cavity, since the lowering of the upper lid associated with the gaze downward would cover most of the pupil. Therefore, it is useful to have an assistant lifting the upper lid during this part of the examination.

3. *Special kinds of examination.* There is a complete interruption in the examination when passing over to one of the following special procedures:

a. Examination in the horizontal optical section for stereoscopic observation of central areas of the fundus in cases of poorly dilated pupils, and for better stereoscopic accessibility of the lateral periphery of the fundus than with the sagittal optical section.

b. Examination with the contact glass with three mirrors (Goldmann) in cases of distorted visibility of the upper and lower periphery of the fundus.

c. Examination with the convex lens for highly myopic fundi.

The examination in the horizontal optical section and that with the convex lens cannot be performed without special adaptations not provided by the ordinary equipment.

III. Constructive principles for biomicroscopy of posterior eye

A. Necessary equipment

1. The *angle of incidence* of the axis of illumination upon the main visual line has to be variable and capable of being sharply reduced (possibility of being swung past the microscope, angle reduction prism).

2. The *system of corneal microscope and*

illumination should be coupled and able of being moved as easily as possible.

3. A *fixation lamp* is necessary to direct the patient's eye indirectly (or directly).

4. A *concave lens* of −58.6 diopters mounted on a proper holder is the most suitable preset lens. It proved to be useful to have a lens that measures at least 19 mm. in diameter and has a plain anterior and a concave posterior face.

B. Desired equipment

1. The *angle of convergence* of the microscopic objectives should be relatively small, not exceeding 10 to 12 degrees.

2. The *disturbing reflections* are avoided by lens coating and,

3. By mounting the preset lens slightly tilted around a frontal axis.

C. Special equipment

1. The possibility of observing in the horizontal optical section is obtained by means of a prism set that can be added to the lamp arm of the slitlamp of Haag-Streit. However, the angle of incidence is invariable (about five degrees).

2. A convex lens of about +58.6 diopters is needed for the stereoscopic examination of the posterior part of the vitreous cavity and of the fundus of highly myopic eyes. Since the convex lens gives an inverse image of the fundus, the distance between the observer's eye and the patient's eye is increased approximately 45 mm. in comparison with the examination by means of a concave preset lens or a contact glass. Therefore, a sufficient motility of the coupled system of corneal microscope and illumination and of the headrest from each other is quite important.

D. Holder of preset lens

There are two different holders for the preset lens; both offer advantages and disadvantages, and thus their desirability is almost equal:

1. The *loose holder of the preset lens* has been carried out with the slitlamp of Haag-Streit: A holder attached to the head rest permits to put the preset lens in front of the patient's eye in any desired position. As a rule, coaxially centered is the most favorable position. If it is necessary to make an examination of the extreme periphery the preset lens can be decentered any time.

To allow alternating use of both the convex lens and the concave lens we have replaced the concave lens on the slitlamp in our clinic by an empty frame into which either the convex lens or the concave lens can be inserted. Also, the sagittal motility of the coupled system of corneal microscope and illumination has been increased by 45 mm.

2. The *holder that centers the preset lens to the corneal microscope* is automatically solved by Carl Zeiss. The preset lens is always in a position well-centered to the corneal microscope by being attached to the latter, maintaining the constant distance from the patient's cornea by means of a "fender" attached to the head rest. Thus the preset lens shares the movements of the microscope in the frontal plane but not in sagittal direction. On the other hand, if the preset lens is allowed to make sagittal movements it is impossible to perform a suitable examination. Such an optical attachment would be a constructive failure.

The distance of the preset lens from the patient's cornea has to be maintained constantly during the examination, but should be brought into the most favorable individual distance prior to the examination. Unfortunately, the possibility of adjusting the glass distance to individual needs has not been provided in the slitlamp of Carl Zeiss. This, and to have the advantage of applying alternately the concave lens and the convex lens, are the reasons why we changed this part of the slitlamp used in our clinic: the small arm of the holder, that allows the preset lens to swing in front of the microscope, has been replaced by a sagittally located socket into which the small band

carrying either the concave or the convex preset lens can be inserted. A small fixation screw permits fastening the small band in sagittally different positions. Thus the preset lens can be brought into the individually needed distance from the patient's cornea prior to the examination.

A holder that centers the preset lens to the lamp arm automatically has to be omitted since this kind of holder inevitably is associated with a constant decentering of the preset lens from the corneal microscope and thus with a disturbing blurring of the image.

If providing nothing but a concave preset lens it is not important what kind of holder actually is preferred. However, with the alternating use of a concave and a convex preset lens, the holder that centers the preset lens to the microscope should be chosen since handling a convex lens with a loose holder would make difficult examining areas of large extent. If one is unwilling to give up the advantages of the loose holder, both kinds of holders can and should be provided.

I feel that there is a definite need for an English explanation of the technique and optical principles of slitlamp study of the posterior eye. By encouraging biomicroscopy of the posterior segment, it is hoped that English-speaking ophthalmologists will demand an English edition of Hruby's monograph.

Alserstrasse 4, (9).

References

El Bayadi: Brit. J. Ophth., **37**:625, 1953.
Funder, W., and Rotter, H.: Arch. f. Ophth., **151**:765, 1951.
Goldmann, H.: Ophthalmologica, **96**:90, 1938.
Hruby, K.: Splatlampenmikroskopie des hinteren Augenabschnittes. Urban & Schwarzenberg, Wien und Innsbruck, 1950.
Littmann, H.: Arch. f. Ophth., **150**:539, 1950; **153**:553, 1953.
Rotter, H.: Arch. f. Ophth., **152**:689, 1952; **156**:503, 1955.

DIFFERENTIAL DIAGNOSIS OF HYSTERIA AND MALINGERING*

In functional amblyopia: Report of a case

Harvey A. Lincoff, M.D., and Jerome Ennis, M.D.
New York

The literature on hysterical blindness was already voluminous when Spaeth[1] reviewed it in 1930. Numerous papers have been published on the subject in the last 25 years, particularly during the second World War. The fact that hysteria and malingering are difficult to distinguish and may often coexist is frequently noted. However, with the notable exception of Gifford's[2] recent paper on psychogenic ocular symptoms, the published material is largely concerned with visual tests to expose the malingerer.

Eggers[3] computed a chart of refractive errors consistent with various visual acuities as an aid in uncovering malingerers. Unsworth[4] detailed methods of provoking confessions, with the proviso that "a psychiatric examination should be obtained on all malingerers to differentiate between neurosis and malingering, and if court martial is ordered it is well that a psychiatrist be present at the trial."

* From the Department of Ophthalmology, New York University-Bellevue Post-Graduate Medical School, and the Division of Child Psychiatry, Mount Sinai Hospital.

More recently, Lewis[5] presented two cases from the civilian population in which the patients had apparent gain from their blindness but about which he hesitated to make a diagnosis of malingering. Marin and Marin[6] felt that the problem was an easier one, and that most cases did not call for psychiatric referral. Yasuna[7] in a very useful paper tabulated the frequency of signs in hysterics, but left unclear whether or not these signs were also present in malingerers.

It is suggested that a diagnosis of functional blindness is the most that can be obtained by the various visual tests. For the further differentiation between the hysteric and the malingerer, other factors must be considered. In the case to be presented, visual testing established the presence of functional amblyopia in a young boy. The patient then admitted that he had profited from his disability, which would seem to indicate that he was a malingerer. Further examination revealed however that the basic disorder was hysterical. The case is felt to be of interest as an example of the differential diagnosis of hysteria and malingering.

Case report

A 10-year-old boy was referred for consultation with the tentative diagnosis of bilateral partial amblyopia of one month's duration. The fields sent by the referring ophthalmologist showed a central scotoma in the right eye of one degree and a similar scotoma in the left eye of five degrees. Both fields also showed a ring scotoma. The vision was 20/70, O.U. The history of the case was:

The child's disability was first noticed by the family physician, who saw the boy squinting at a picture in his office and asked him if he had any difficulty in seeing. The boy answered uncertainly that he thought he could not see well. Testing with a Snellen chart at that time revealed the uncorrected vision to be 20/70, O.U. The boy was then refracted by an optometrist, who found the refractive error to be negligible but confirmed visual acuity as 20/70.

The child was referred to an ophthalmologist, who did a complete examination including a series of field studies, and found the central and ring scotomas already referred to. The fact that the child had suffered a supposedly minor brain concussion two years previously was now seriously reconsidered, and he was referred for neurologic examination, skull X-ray studies, and electroencephalographic studies, all of which proved negative. These studies consumed two months.

At this point it was decided to bring the child to New York for further perimetric and neurologic studies. The tentative diagnosis was bilateral central amblyopia, secondary to possible intracranial disease or retrobulbar neuritis.

The patient appeared for examination as a self-composed, well-mannered boy. His attitude was quiet, and he was completely cooperative. There was no anxiety present. Visual testing on the Snellen chart was 20/70, O.U. The child made an effort to read the 20/50 line, but misread all the letters.

The external eyes were negative, the media were clear, the discs were a healthy pink color, the central area appeared entirely normal, as did the rest of the retina. Extraocular movements were normal. The neurologic examination was negative.

The initial field studies went as follows:

The child was seated at a Harrington perimeter and remarked that this one was somewhat different from the one he had been tested on by the ophthalmologist in his home town. Little explanation of the method was necessary, as the child quickly indicated that he understood how the field was done and what was expected of him. With a 3/330 white test object the initial field gave a ring scotoma between 30 and 40 degrees and a central scotoma of 10 degrees in both eyes (fig. 1). Repeat fields with a 1/330 white, 5/330 white, and 10/330 white showed erratic and inconsistent variation in the position and thickness of the ring scotoma. For example, the scotoma narrowed with the 1/330 white and broadened with the 10/330 white. Again, it shifted from between the 30

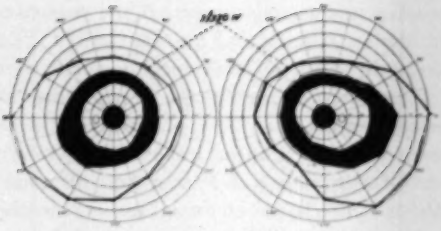


Fig. 1 (Lincoff and Ennis). With a 1/330 white test object the initial field gave a ring scotoma between 30 and 40 degrees and a central scotoma of 10 degrees in both eyes.

and 40 isopter to between the 40 and 50 isopter, even though fixation was noted to be constant. The central scotoma of 10 degrees on the perimeter remained unchanged with all test objects.

The child gave every indication that he was doing his best to answer properly. Central fields on the tangent screen showed a five-degree central scotoma in both eyes (fig. 2). The blindspot was normal. The child was tested at one meter and two meters and always showed a five and a two and one-half degree central scotoma on the tangent screen. Variations in the size or color of the test objects at any one distance also did not affect the size of the scotoma.

The inconsistencies in the peripheral field, the improbability of seeing 20/70 with a five-degree central scotoma, and the classic proof offered by the projection of a scotoma of the same linear diameter at one and two meters, indicated that the field was functional.

The child was again placed before the Snellen chart and asked to read. He read as far as 20/70 as he had before, mistaking the letters on the 20/50 line. A trial frame was placed on his face with a combination of pinholes and multiple lenses which neutralized each other. It was suggested to him that this was a telescope which would bring the smaller lines gradually into view by magnifying them. With each addition of a pair of lenses which neutralized each other it was suggested that he might read the next line, and in each case he succeeded in doing so until he read the 20/15 line with each eye. Nothing further was done on this day.

The total absence of anxiety suggested that the mechanism of this case of functional amblyopia was hysterical. The malingerer is more inclined to exploit his symptoms in an exaggerated manner to try to convince the doctor of the reality and seriousness of his visual defect. He simulates the apprehension with which the ophthalmologist is familiar in the organic cases which he sees.

At the next examination the child was told that his vision had returned to normal, and he was asked what he thought about this apparent change. He replied simply that he must have become better. There was neither elation nor embarrassment in his manner, the reactions which would be expected from the organic case and the malingerer, respectively. It was noted, however, that for the first time the child appeared anxious. He was asked to talk further about the period of his seeing difficulties, and he spontaneously presented the following material:

He spoke first about his relationships with the other children at his school. He was not usually one of those selected to play in the noon pick-up baseball games, and he felt that certain of the children looked down on him. He then mentioned that he had recently received a mark of 60 in reading. He felt that this low grade had caused a loss of prestige for him among the children. He remarked that the low grade in reading might have been attributable to his seeing difficulties. Further, he recalled having thought that these difficulties might arouse sympathy toward him on the part of his schoolmates.

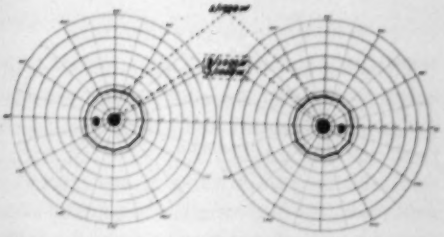


Fig. 2 (Lincoff and Ennis). Central fields on the tangent screen showed a five-degree central scotoma in both eyes.

This amounted to a realization on his part that his recent visual defect had been of some advantage to him.

He was asked about the beginning of his visual loss, first noted in the office of the family physician. It was apparent that he had not consciously planned any deception, but that the doctor's questions as to whether he could see crystallized and reinforced the neurotic solution of his problems which was already manifested by the squinting.

It is of interest that during the course of the investigation in his home town he was aware from time to time that his visual disability was of value to him; that is to say, he occasionally realized the advantages mentioned in regard to his problems at school. But as the investigation gained momentum and more and more physicians became involved, and his parents' concern increased, the awareness of these advantages occurred to him less and less frequently. It was necessary for him to deal with his guilt over these advantages by repressing all thought of them.

It was explained to the boy that while his problems at school were real ones, which required working out, the apparent advantages of his visual defect over which he had so much conflict were in reality of doubtful value. It was pointed out that if he really were blind, he would never be able to play baseball again and that, although his misfortune might arouse momentary sympathy in his friends, they would soon lose interest in his handicap, which would in the end further limit his relationships with them. The child appeared to find this interpretation reasonable.

Evolution of the scotomas

The child was further questioned in an attempt to discover how he had, in a sense, designed the central and ring scotomas of the initial fields, which unlike the constricted field are very rare in cases of hysteria. This appears to have occurred in much the same way as his original failure to see at the "suggestion" of his family physician.

The ophthalmologist who did the first field studies unwittingly suggested the scotomas by saying as he moved his test object, "You see, you see, you don't see, do you?" His expectations of finding the central scotoma which occurs in cases of relative amblyopia were evidently transmitted to the child. We can only speculate about the ring scotomas. Probably a chance equivocal answer on the part of the child caused the physician to concentrate on this area, as a result of which the child was encouraged to produce the remainder of the scotoma. It is apparent that the patient is an extremely suggestible child, who, as we now know, had reasons for not wanting to see.

The further disposition of the case had now to be decided. To summarize what had so far been accomplished, the partial blindness from which the child had suffered for several months had been shown to be functional and it had been decided that the mechanism of the blindness was hysterical. In a friendly, nonthreatening relationship with the ophthalmologist, and at the latter's suggestion, the child accepted the fact that he could now see. With the loss of his symptom his indifference disappeared and was replaced by anxiety.

It might be argued that the boy's newly evidenced anxiety was fear about the consequences of his blindness being uncovered as functional. He did, in fact, ask at one point what the examiner was going to tell his mother. In answer to this it can be said that the child's anxiety did not seem attached to such a fear. He did not dwell on possible consequences of his mother being told but asked about it almost incidentally. His thoughts seemed to be centered elsewhere.

His spoken thoughts were about his school problems, as detailed above. It might also be suggested that these problems were the basis of his anxiety and symptom formation. There is no doubt that he thought to benefit at school with his blindness. He admitted this. If this were the whole, the case for conscious deception, that is, malingering, would be a strong one.

Evidence to the contrary is provided, however, by the unconscious manner in which the symptom developed. It will be recalled that the blepharospasm which preceded all the other symptoms was one about which the child had no awareness at all. Again, his behavior throughout had an unnatural indifference not designed to convince. Finally, his anxiety did not seem sufficiently attached to his problems at school, even as he spoke of them. The gain which he thought to obtain in this regard appeared to be of a *secondary* nature. Beneath this there seemed to be *primary* problems about which he did not speak.

In order to establish the primary cause of the child's anxiety, and to treat it, he was referred to a psychiatrist. An evaluation of the psychiatric findings follows:

Psychiatric history

The developmental history includes a previous episode of abdominal symptomatology, diagnosed and treated as juvenile duodenal ulcer, although X-ray evidence of the crater was never found. This is suggestive of a prior episode of hysteria.

The patient is the younger of two children in a middle-class family. He has a 16-year-old sister. The mother is an attractive and vivacious but immature person, who is inconsistent in her relationships, at first seductive but finally anxious about and rejecting people. She is a self-centered woman and favors her daughter to the patient, as an egotistical extension of herself. The father is a quiet, retiring man, who is somewhat detached from his family and who occasionally, in order to assert himself, become excessively disciplinary with his son. His wife, however, is the dominant figure.

The child has an intense, unsatisfied need for his mother, and feels both uncertain of her affection and guilty because of the extreme rivalry with his sister in this regard. His father is periodically capable of severely frightening him. This is a family situation likely to produce an anxious child, suffering from feelings of rejection and inadequacy in his relations with schoolmates, as well as in his relations with his family.

On examination, the patient was found to be a bright, tense boy who feels threatened by the interpersonal environment already described, and who constricts and supresses his emotional involvement with it in order to defend himself against it. Psychologic testing also revealed frightening and consciously unacceptable sexual fantasies. It specifically indicated that he had, actually or in fantasy, recently witnessed a sexual act of his parents, a scene at once stimulating, forbidden, and frightening.

Psychiatric formulation

The latter visual experience precipitated the hysterical partial loss of vision because the child was threatened by the emergence of unacceptable sexual and hostile impulses. His defenses against these anxiety-provoking impulses had previously been mostly successful in that the impulses had been repressed. This resulted, however, in a timid, constricted, and easily shamed personality. Now the impulses might break through into consciousness, having been reinforced by the emotions stimulated in witnessing the forbidden scene.

When the child was first asked whether he had difficulty in seeing, he unconsciously accepted the suggestion that he did, because such a symptom offered a solution to his psychologic dilemma. The symptom meant, "I cannot see because I have seen and want to see something forbidden." Such a solution was already spontaneously evolving and was responsible for the blepharospasm noticed by the family physician whose remark facilitated and accelerated the process.

Function of the hysterical symptom

Conversion hysteria is a psychoneurosis whose symptoms are unconsciously produced. It is this unconscious production of symptoms which differentiates hysteria from malingering; in malingering, physical signs or symptoms are consciously counterfeited. Behavior can, however, be purposeful even without conscious recognition of this fact.

Although unconsciously determined, the symptoms of hysteria provide partial protection against the anxiety generated by repressed conflicts, as well as a disguised, symbolic expression of them. Sensory hysterical symptoms are usually unconscious rejections of emotionally disturbing perceptions.

Hysterical visual symptoms are expressions of repressed desires to see forbidden things. This, as previously described, seems to be the basis of our patient's symptomatology. Thus, the primary function of hysterical blindness (or any other hysterical symptom) is to help the patient adapt to the stress produced by unconscious impulses. Hysterical symptoms are attempts to solve emotional conflicts in physical terms. Such adaptations are often crippling but represent the best adjustment of which the individual is capable.

Secondary gain

The uses a patient can make of a neurotic illness, which are not necessarily connected with its origin, are called the secondary gains of illness. It must be stressed that such gains are the advantages of illnesses and not the causes of them. Patients are to varying degrees consciously aware of such uses of symptoms. Secondary gains may be the pity, love, attention, help, excuse for failure, and so forth, obtained by the utilization of neurotic symptoms. They are unusually prominent in hysteria, although they occur in all illnesses, physical as well as emotional. Although not the cause of hysteria, the secondary gains are often obstacles to its successful treatment because patients are unwilling to give up illnesses which are of such advantage to them.

Our patient's expectation of greater acceptance by friends and of an excuse for his poor reading constituted the secondary gains of his hysterical partial blindness. The increased attention and care he received from his mother, and the greater indulgence shown him by his father, both as a result of his illness, constituted further important secondary gains.

Treatment formulation

In terms of the just described mechanisms of hysteria, the treatment which proved symptomatically successful may be described as the giving of strong suggestions which were accepted because of the positive and authoritative, but nonthreatening relationship of the ophthalmologist to the patient. This was reinforced by the doctor's interpretative minimization of the secondary gains. Neither the underlying cause of the illness nor the reason it had to be put to such secondary uses was fundamentally modified.

After the symptomatic remission, psychologic testing revealed the re-establishment of the patient's previous unhealthy personality patterns and defenses. The course of his illness with its varying responses to different kinds of medical management emphasizes the danger of fixating psychogenic ocular symptoms during the course of a prolonged physical work-up.

Differential diagnosis

The differential diagnosis of hysteria and malingering is theoretically clear-cut. It is the difference between simulation in malingering and unconscious determination in hysteria. In practice, however, the delineation is not always so sharply and easily made, since there are varying degrees of awareness of the secondary gains in hysteria. The uses a patient puts his symptoms to may be so obviously advantageous that it is felt he must be simulating the symptoms for this purpose. Such gains, it must be re-emphasized, are secondary.

Regular confusion between the two conditions is most likely to be made by those who mistakenly consider all hysterics as malingerers, who can volitionally control their symptoms. Discrepancies, contradictions, bizarre exaggerations of symptoms, are suggestive of malingering. The absence

of much anxiety about symptoms, as in this case, is indicative of hysteria. The reoccurrence of anxiety following the cure of the visual defect further indicates the defensive nature of the symptom and reinforces the impression of hysteria, as does the patient's extreme suggestibility, indicated by his initial iatrogenic and later therapeutic responsiveness.

Finally, data from the history and psychologic testing reveal evidence of much repression of anxiety-provoking impulses, a finding always present in hysteria.

30 East 40th Street.

We wish to express our appreciation for clinical material contributed by Dr. Joseph B. Cramer, associate professor of child psychiatry at Albert Einstein College of Medicine.

References

1. Spaeth, E. B.: Arch. Ophth., **4**:911-918 (Dec.) 1930.
2. Gifford, E. S.: Arch. Ophth., **53**:318-329 (Mar.) 1955.
3. Eggers, H.: Arch. Ophth., **33**:23-27 (Jan.) 1945.
4. Unsworth, A. C.: Am. J. Ophth., **28**:148-159 (Feb.) 1945.
5. Lewis, P. M.: Am. J. Ophth., **31**:870-871 (July) 1948.
6. Marin, A., and Marin, E.: Am. J. Ophth., **32**:450-451 (Mar.) 1948.
7. Yasuna, E. R.: Arch. Ophth., **45**:70-76 (Jan.) 1951.

Additional bibliography

Burch, E. P.: Psychoneurotic reaction patterns in ophthalmology. Tr. Am. Ophth. Soc., **48**:370-394, 1950.

Ellmore, E.: A study of psychic blindness. Psychoanalyt. Rev., **23**:399-403, 1936.

Freud, S.: Psychogenic visual disturbance. In Collected Papers of Sigmund Freud, Vol. II. London, Hogarth Press, 1948.

Harrington, D. O.: Psychosomatic interrelationships in ophthalmology. Am. J. Ophth., **31**:1241, 1948.

Huebsch, D. E.: Psychoanalysis and eye disturbances Psychoanalyt. Rev., **18**:166-180, 1931.

THE REMOVAL OF SCLEROCORNEAL SUTURES

Brian J. Curtin, M.D., and Truman L. Boyes, M.D.
New York

During the past few years there has been a decided increase in the use of border-to-border sutures in cataract surgery. The removal of such sutures can be extremely troublesome, and the procedure is often approached by patient and surgeon alike with considerable misgiving. Because of the severity of its complications, the removal of these sutures should be considered an important part of the cataract operation.

Indications for suture removal

It is generally agreed that the sclerocorneal suture should normally be removed anywhere from the 11th to the 14th postoperative day. A suture in some instances may be permitted to slough out, if necessary, without undue danger to the eye. A suture, however, must be removed when it becomes the focus of a pathologic process. Thus infection, in the form of a stitch abscess, necessitates prompt removal.

In addition, if the suture acts as a filtering wick for aqueous, with partial or total loss of the anterior chamber, its immediate removal is indicated. The presence of a filtering wick can be difficult to ascertain. Occasionally some edema of the surrounding conjunctival flap is present, but conclusive evidence of the condition can be obtained

by use of either of the fluorescein tests. In the topical test, one drop of a two-percent solution is placed directly on the suspected suture under biomicroscopy. A light green rivulet appears in the orange-stained area, if filtration exists. Possibly more conclusive is the systemic fluorescein test, in which five to 10 cc. of a five-percent solution is injected intravenously with the patient at the slit-lamp. Seconds later, when the dye reaches the anterior chamber, filtration can be detected as the green-colored aqueous appears about the suture on the conjunctival surface.

Complications

The complications of suture removal are wound rupture, infection, and loss of anterior chamber.

1. *Wound rupture* may be of three degrees as outlined by Gradle and Sugar.[1] The first degree consists of gaping of the wound usually with edema of the conjunctival flap. In the second degree there is definite rupture of the wound with tearing of new blood vessels and resultant hyphema. Third-degree rupture is accompanied by either iris or vitreous prolapse. These various stages of wound rupture are a sequel to traumatic instrumentation or occur as a result of lid squeezing and eye movement during removal by an improperly prepared patient.

2. *Infection* ranges from corneal abscess to panophthalmitis, which ensues as a result of virulent pathogenic bacteria entering the suture tract following removal. Fortunately this event is rare.

3. *Loss of anterior chamber* occurs as a result of wound rupture. It also follows the removal of a sclerocorneal suture that is placed too deeply so that its tract is in communication with the anterior chamber. In such an instance its removal can be followed by loss of aqueous along the tract and concomitant flattening of the anterior chamber.

Hughes and Owens,[2] in their cataract series, estimate that of a total 3.2 percent loss of anterior chamber, 49 percent occurred during or immediately after suture removal. They conclude that this complication can partially be avoided by a longer, more superficial bite in inserting the sutures. Attention to this technical detail has other advantages, for such a suture can be removed more easily by virtue of its wider loop, and its superficial bite lends itself to a better depth of anesthesia.

Removal of sutures

A. Preparation of patient

As a precaution against infection, it is advisable to have the patient use an antimicrobial solution for a few days prior to suture removal. In addition, the conjunctival sac should be thoroughly irrigated immediately prior to the procedure. Undoubtedly the most important safety factor is adequate anesthesia. The topical use of such solutions as pontocaine, butyn, or cocaine are rarely sufficient. Application of pledgets containing these solutions effect little additional anesthesia. In contrast to these the use of powdered cocaine, phenacaine, or pontocaine (niphanoid), as recommended by Kirby,[3-5] rarely fails to produce the proper depth of anesthesia. After the sutures are cleaned of all mucus with a cotton swab, the powder is placed directly upon the suture and allowed to dissolve in situ. The excess is then irrigated from the conjunctival sac.

While the average patient will fully cooperate if anesthesia is adequate, in certain apprehensive patients it is advisable to rely upon sedation and akinesia from the outset. Demerol intramuscularly in doses of 50 mg. usually produces the desired sedation and analgesia. Barbiturates, however, will often suffice. Of utmost importance is the akinesia of the orbicularis. This can be achieved by the injection of either procaine or lidocaine in the manner of Van Lint or O'Brien. Special care must be taken that the patient does not squeeze the lids during these injections.

B. Technique of removal

The following equipment is needed: cotton swabs, a delicate tissue forceps, and scissors. It is preferable to use a spring scissor with

sharpened points. Using such an instrument, the surgeon can rest his hand comfortably during the procedure and, thereby, his handling of the scissors becomes more deft and accurate. A spring iris scissors is preferred by the authors although a DeWecker[6] or Westcott with sharpened points (stitch scissors) are both excellent. Harrison's[7] scissors, which were designed especially for this purpose, are equally useful.

Initially the patient is directed to look down. An assistant retracts the upper lid with either fingers or a retractor. A thin cotton pad will help if fingers are used. If the suture is loose, it can be teased up with a cotton swab and the surgeon, working from below, severs the lower arm of the suture loop. This is best accomplished by placing one tip of the scissors blade between the two suture arms at an angle of no greater than 45 degrees to the line of the suture.

The temporal suture should be cut from the temporal side, the nasal suture from the nasal side (fig. 1). The rationale in the approach, as first enunciated by Hilding,[8] lies in the fact that should the patient suddenly look up, the suture arm can slip past the scissor blade unimpeded. Furthermore, the incision, lying above the instrument, cannot be traumatized as the eye moves upward.

If the suture cannot be teased into position, a forceps must be used. The forceps is held in the horizontal plane and the suture grasped with an absolute minimum of pressure. The suture should be able to slip out of the forceps grasp with any movement of the eye. A delicate tissue forceps is best suited to this end. If one arm cannot be severed, the knot is then cut as suggested by Guyton[9] and one presenting end of the suture grasped and withdrawn.

If grasping the severed end entails any amount of trauma to the eye, it is advisable to allow healing to progress a week or so and then, with the reduction in reaction coupled with the natural tendency of tissues to extrude foreign material, the remnant can usually be grasped.

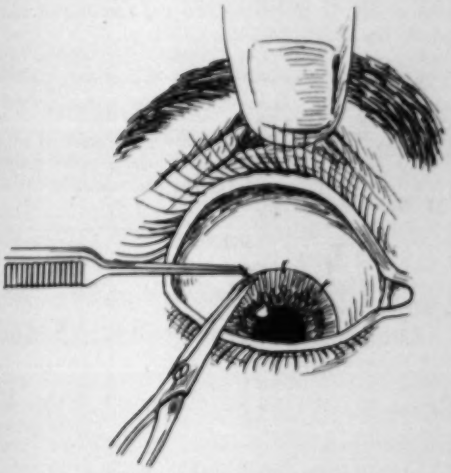


Fig. 1 (Curtin and Boyes). Technique for removal of temporal suture, O.D.

After removal of the suture, a local antimicrobial solution is instilled and a patch applied to the eye for 24 hours.

Results

This method of suture removal has proved most successful over the past two and one half years of its use by us. In more than 200 cataract cases in which two or more sclerocorneal sutures were used this method has been employed without complications to date. In addition to this, in all but four or five cases, the anesthesia was of such a degree that the patient experienced no discomfort whatsoever. This combination of complete anesthesia for the patient and lack of anxiety for the surgeon makes the procedure a pleasant contrast to the painful, complication-prone procedure it can sometimes be.

654 Madison Avenue (21).

References

1. Gradle, H. S., and Sugar, H. S.: Wound rupture after cataract extraction. Am. J. Ophth., **25**:426 (Apr.) 1942.

2. Hughes, W. F., Jr., and Owens, W. C.: Postoperative complications of cataract extraction. Arch. Ophth., **38**:577 (Nov.) 1947.

3. Kirby, D. B.: Prevention and handling of complications arising during and after cataract extraction. Arch. Ophth., **25**:866 (May) 1941.
4. ———: Surgery of Cataract. Philadelphia, Lippincott, 1950, pp. 603-604.
5. ———: Advanced Surgery of Cataract. Philadelphia, Lippincott 1955, pp. 99-100.
6. Stallard, H. B.: Modern Trends in Ophthalmology. (Arnold Sorsby, Editor.) New York, Hoeber, 1955, p. 283.
7. Harrison, W. J.: Instrument for removal of sutures. Am. J. Ophth., **35**:1207 (Aug.) 1952.
8. Hilding, A. C.: Removal of sclerocorneal sutures. Arch. Ophth., **24**:371 (Aug.) 1940.
9. Guyton, J. S.: Prevention and management of complications of cataract extraction. Am. J. Ophth., **31**:1085 (Sept.) 1948.

ETHYLENE-OXIDE STERILIZATION IN OPHTHALMOLOGY*

R. A. SKEEHAN,† JR., LT. COL., (MC), J. H. KING,‡ JR., M.D.,
AND
SAUL KAYE,§ A.B.
Washington, D.C.

Sterilization of ophthalmic instruments and equipment is a major concern in the daily practice of ophthalmology. For sharp instruments, various solutions such as benzalkonium chloride and Bard-Parker Formaldehyde Germicide solution have been utilized. Other instruments are autoclaved or subjected to high pressure steam in order to be rendered sterile. Ultraviolet irradiation of various instruments is of questionable efficacy.

Rendering sterile an entire hand slitlamp, a metal locator probe (Berman) and cord, a giantscope, or an ophthalmoscope by heat or soaking would certainly damage or destroy these items. An ideal sterilizing agent for such items would be a noncorrosive and nondamaging gas which would diffuse through all types of porous substances, which could easily be removed by simple aeration following treatment, and which could effectively destroy all forms of micro-organisms at ordinary temperatures. In addition, other desirable features would include rapid action, low toxicity to human beings, noninflammability, ease of handling and storage, and ready availability.[1]

When the sterilizing properties and desirable characteristics of gaseous ethylene oxide became known, studies were begun to determine if there was a practical method of employing this type of sterilization in ophthalmologic practice.

Ethylene oxide (also known as 1, 2-epoxyethane and oxirane) is the simplest of the epoxy compounds which are molecules containing two carbon atoms and an oxygen atom linked together in a three-membered ring. Such compounds are very reactive.

The chemical structure of ethylene oxide is $CH_2 - CH_2$ with an oxygen bridging the two carbons.

Ethylene oxide has a specific gravity of 0.8838 10/4 C. It boils at 10.8°C., and freezes at −111.3°C. It is a gas at ordinary temperatures and pressures, but is easily liquified. It is soluble in all proportions in water, alcohol, and ether. The gas has a rather pleasant ethereal odor. It is highly flammable and the vapors form an explosive mixture with air in all proportions from three to 100 percent by volume. This explosive danger is eliminated, however, when the gas is mixed with more than 7.15

* From the Ophthalmology Service, Walter Reed Army Hospital, and the Ocular Research Unit, Walter Reed Army Medical Center.
† Ophthalmology Service, Walter Reed Army Hospital.
‡ Chief, Ophthalmology, Washington Clinic, clinical associate professor of ophthalmology, Georgetown University Medical School.
§ U. S. Army Chemical Corps, Camp Detrick, Maryland.

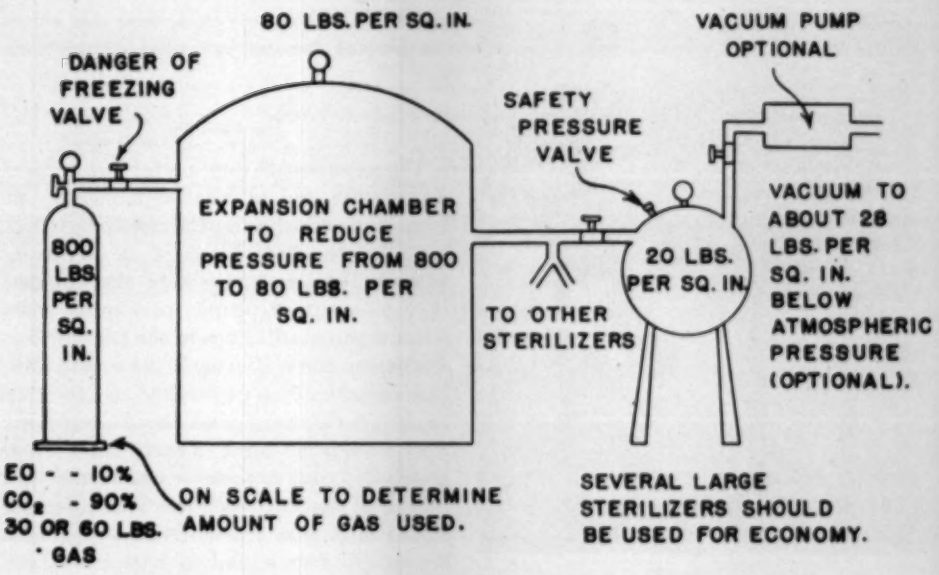

80 LBS. PER SQ. IN.
VACUUM PUMP OPTIONAL
DANGER OF FREEZING VALVE
SAFETY PRESSURE VALVE
EXPANSION CHAMBER TO REDUCE PRESSURE FROM 800 TO 80 LBS. PER SQ. IN.
800 LBS. PER SQ. IN.
20 LBS. PER SQ. IN.
VACUUM TO ABOUT 28 LBS. PER SQ. IN. BELOW ATMOSPHERIC PRESSURE (OPTIONAL).
TO OTHER STERILIZERS
EO - - 10%
CO_2 - 90%
30 OR 60 LBS. GAS
ON SCALE TO DETERMINE AMOUNT OF GAS USED.
SEVERAL LARGE STERILIZERS SHOULD BE USED FOR ECONOMY.
CARBOXIDE STERILIZING APPARATUS

Fig. 1 (Skeehan, King, and Kaye). Carboxide sterilizing apparatus.

times its volume of carbon dioxide. A commercial product is manufactured (Carboxide®)* consisting of 10-percent ethylene oxide and 90-percent carbon dioxide. This combination can be mixed with air in any proportion without forming an explosive mixture. Carboxide is available in large gas cylinders containing either 30 or 60 pounds of gas under about 800 pounds per square inch pressure. Use of this mixture in a sterilizing chamber requires an expansion chamber to avoid fractionation of the mixture and to reduce the pressure to about 80 pounds per square inch after which it can be admitted to the sterilizer.* It is possible to admit short bursts of Carboxide directly into the sterilizer, but control is difficult, the valves may freeze, and the proportions of carbon dioxide and ethylene oxide are not uniform (fig. 1). For the purposes for which this gas was to be used in ophthalmology, such as apparatus would be too bulky and expensive.

It was found that the Army Chemical Corps was using a new and more convenient method of gaseous ethylene oxide sterilization. The ethylene oxide was mixed with dichlorodifluoromethane (Freon-12) instead of with carbon dioxide, there being 18.75 percent ethylene oxide and 81.25 percent dichlorodifluoromethane in a 12-ounce sealed can under about 55 pounds per square inch pressure. The can thus contains about 75 cc. of ethylene oxide in the liquid state.

The contents of the can are easily admitted to the sterilizer by means of a needle valve† to which the can is screwed, top down, to permit flow of all liquid into the inlet port. The liquid mixture immediately expands to a gaseous form on entering the tubing to the inlet port of the sterilizing

* Carboxide, product of Carbide and Carbon Chemicals Corporation, Passaic, New Jersey.

* American Sterilizer Company, Erie, Pennsylvania.

† Can-O-Gas valve, manufactured by the Virginia Smelting Company, West Norfolk, Virginia.

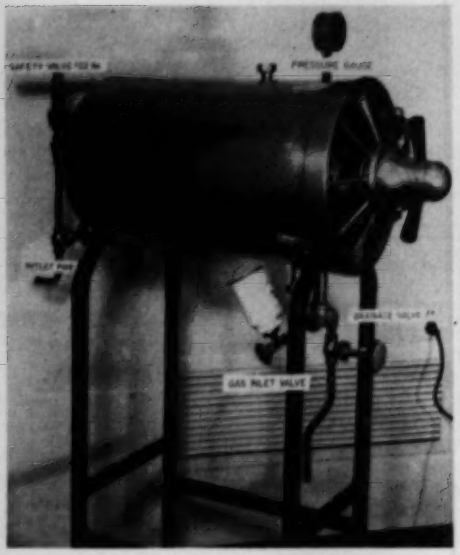


Fig. 2 (Skeehan, King, and Kaye). Modified steam sterilizer.

chamber. No previous exhaustion of air is necessary.

An old or discarded small steam sterilizer can be easily modified so that the vapor enters through the former condensate return line (fig. 2). A short length of pipe with a valve is also fixed to the entrance port. The former steam inlet line is fitted with a pipe and valve for exhaust. A safety valve adjusted to 22 pounds per square inch, and a pressure gauge for measuring positive and negative pressures, complete the attachments to the sterilizer (fig. 3).

A vacuum pump can be used on the rear outlet pipe to wash the contents of the chamber with sterile air admitted through a filter attached to the side pipe of the entrance port. However, it has not been found necessary to aerate the materials which have been sterilized. Instruments are double wrapped in linen and about 30 minutes' exposure to room atmosphere suffices to rid the materials of all discernible traces of ethylene oxide. There is no difficulty in maintaining proper concentration of ethylene oxide since the entire contents of the can are used during each run.

Procedure

The experiments were performed at room temperature and at relative humidities of from 20 to 35 percent. Moisture is necessary for ethylene oxide to exert its sterilizing action.[2] The pressure within the chamber rises to about 22 pounds per square inch. After a period of 12 hours, the pressure has dropped to about 10 pounds per square inch, indicating that the gas slowly escapes even from a well sealed chamber. Experiments were conducted using Pseudomonas aeruginosa, a very common contaminant, and spores of Bacillus globigii. The latter are among the most resistant micro-organisms known. Six-hour exposures were carried out at first.

Controls were run simultaneously on contaminated cardboard spatulas, cellophane disposable eyedroppers, and glass and metal not exposed to ethylene oxide vapors. These demonstrated that sufficient organisms survived the six-hour period at normal room temperature and humidity to rule out the possibility of negative cultures due to spontaneous death of all the organisms (tables 1 and 2). The quantity of micro-organisms placed on each test site was equal to or greater than that

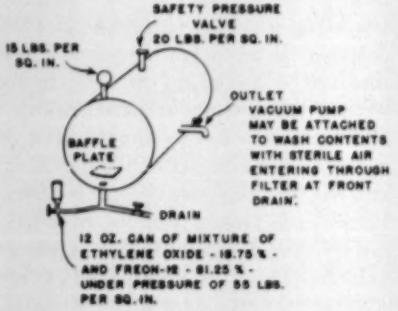

SAFETY PRESSURE VALVE
20 LBS. PER SQ. IN.
15 LBS. PER SQ. IN.
OUTLET
VACUUM PUMP MAY BE ATTACHED TO WASH CONTENTS WITH STERILE AIR ENTERING THROUGH FILTER AT FRONT DRAIN.
BAFFLE PLATE
DRAIN
12 OZ. CAN OF MIXTURE OF ETHYLENE OXIDE - 18.75 % - AND FREON-12 - 81.25 % - UNDER PRESSURE OF 55 LBS. PER SQ. IN.

Fig. 3 (Skeehan, King, and Kaye). Freon-ethylene oxide sterilizing apparatus.

TABLE 1

DEATH RATE IN SIX HOURS OF PS. AERUGINOSA AND B. GLOBIGII SPORES ON ARTICLES NOT EXPOSED TO ETHYLENE OXIDE

Type of Article	Immediately after Contamination		Six Hours after Contamination	
	Total B. globigii Recovered	Total Ps. Recovered	Total B. globigii Recovered	Total Ps. Recovered
Spatula	7,600	31,500	4,750	35
Eyedropper	1,610	364,000	1,110	2,800

found after direct contact with a frankly purulent lesion.

Relatively inaccessible areas on various ophthalmic instruments were chosen as test sites for contamination by Bacillus globigii and Pseudomonas aeruginosa. In order to be certain that a significant number of organisms were implanted on each area, a duplicate test site was contaminated in each area and, after drying, sterile swabs were rubbed over these latter sites and the swabs broken off into tubes of sterile nutrient broth. In every case there was growth, thus indicating that the instruments were actually contaminated. The various items, double wrapped in kraft paper, were then exposed to ethylene oxide vapor in the concentration of 1.25 ml. per liter for six hours. At the end of that time each of the original sites was swabbed as above. Table 3 and 4 show the results of six-hour exposure to ethylene oxide vapor. In no case was there a positive growth on plates or in nutrient broth.

Further studies were made with contaminated cellophane disposable eyedroppers and paper spatulas packed in cardboard boxes. These droppers and spatulas are used routinely in our clinic to apply solutions and ointments to individual eyes and to prevent contamination of various medications as demonstrated by King.[8] Some boxes were sealed in cellophane and some were left unwrapped. In both cases, there was complete sterilization (table 5).

Many other trials were made in order to double check the results and to determine the minimum time necessary for complete sterilization at room temperature. Pseudomonas aeruginosa, Bacillus globigii, and Bacillus subtilis were used as test organisms. It was found that exposure to the ethylene oxide-dichlorodifluoromethane mixture for less than two hours and 15 minutes always resulted in incomplete sterilization, but that exposure for three hours always resulted in negative cultures. In most cases, two and a half hours would render the test objects sterile.

Separate investigations had shown that by increasing the temperature of the sterilizing chamber by 10°C. the exposure time was halved. Also, doubling the concentration of the ethylene oxide doubled the effectiveness.

In order to provide a wide margin of safety our items are exposed to the ethylene

TABLE 2

DEATH RATE IN SIX HOURS OF PS. AERUGINOSA AND B. GLOBIGII SPORES ON SURFACES NOT EXPOSED TO ETHYLENE OXIDE

Surface	Immediately after Contamination		Six Hours after Contamination	
	Total B. globigii Recovered	Total Ps. Recovered	Total B. globigii Recovered	Total Ps. Recovered
Glass	5,750	1,200,000	7,110	7,000
Metal	2,465	700,000	2,395	1,760

TABLE 3

THE STERILIZATION OF OPHTHALMIC INSTRUMENTS BY EXPOSURE TO ETHYLENE OXIDE VAPOR: TEST ORGANISM B. GLOBIGII SPORES
(1.25 ml./liter for six hours)

Instrument	Site	Before Exposure to Ethylene Oxide	After Exposure to Ethylene Oxide
		Total B. globigii Recovered	Total B. globigii Recovered
Ophthalmoscope	Body	4,200	0
Cautery	Plastic	1,480	0
Scissors	Center	500	0
Loupe	Lens	1,600	0
Magnet	Cord	2,240	0
Magnet	Tip	1,410	0
Locator, Berman	Plastic tip exterior	1,620	0

oxide vapor in the sterilizing chamber for four hours. Table 6 shows the results on culturing test sites on metallic surfaces at 70°F. (25°C.) after two- and four-hour exposures compared to exactly similar sites not so exposed and used as controls. Controls in all experiments were always positive. Fourteen test sites, using seven organisms for each of the three exposure periods, show that sterility is assured after four-hour contact with ethylene oxide vapor.

In our operating room we have sterilized and used the following instruments: hand magnet, loupes, binocular microscope, hand slitlamp, the Berman locator probe, transformers, hand battery cautery (Hildreth), keratomes, scissors and other sharp instruments, ophthalmoscopes and giantscopes, and tonometers. There is no physical change in the various items exposed to the gas. Heat, for example, will eventually discolor and crack plastic parts, but there is no change in the appearance or usefulness of plastic items after multiple exposures to ethylene oxide. No additional cleansing, rinsing, or neutralizing of the sterilizing agent from the instruments is necessary. Consequently, there is no danger that an irritating chemical might be introduced intraocularly or topically by means of a surgical instrument.

TOXICITY

The toxic limits of ethylene oxide for human beings are about the same as those for ammonia.[1] In low concentrations the gas does not possess a distinct odor, but it is

TABLE 4

THE STERILIZATION OF OPHTHALMIC INSTRUMENTS BY EXPOSURE TO ETHYLENE OXIDE VAPOR: TEST ORGANISM PS. AERUGINOSA
(1.25 ml./liter for six hours)

Instrument	Site	Before Exposure to Ethylene Oxide	After Exposure to Ethylene Oxide
		Total Ps. Recovered	Total Ps. Recovered
Ophthalmoscope	Body	98,000	0
Cautery	Terminals	790	0
Scalpel	Blade	162,000	0
Tonometer	On shaft, slipped back into base	30,000	0
Loupe	Lens	168,000	0
Magnet	Body	136,000	0
Locator, Berman	Tip, covered by plastic tip	700,000	0

TABLE 5

STERILIZATION OF ARTICLES CONTAMINATED WITH B. GLOBIGII SPORES OR PS. AERUGINOSA BY EXPOSURE TO ETHYLENE OXIDE VAPOR
(1.25 ml./liter for six hours)

Type of article	B. globigii		Ps. aeruginosa	
	Total Organisms Recovered	Nutrient Broth	Total Organisms Recovered	Nutrient Broth
Spatula	0	No growth	0	No growth
Eyedropper in unsealed box	0	No growth	0	No growth
Eyedropper in cellophane-sealed box	0	No growth	0	No growth

sufficiently irritating to give warning of its presence. Reported cases list headaches, nausea and vomiting, and respiratory irritation as symptoms, but no permanent ill effects occurred.[4] In the small amounts used in a 35- or a 60-liter capacity sterilizer, the probability of untoward reaction in human beings exposed to exhausting gas is remote, but, as a precaution, the outlet pipe should be led outside the building. Cases of accidental blistering of the skin due to exposure to ethylene oxide vapor have occurred. While the liquid when spilled on the skin evaporates rapidly and without causing damage, burns occurred when rubber shoes and rubber gloves were worn by laboratory

TABLE 6

STERILIZATION OF CONTAMINATED METALLIC SURFACES BY ETHYLENE OXIDE VAPOR
(1.25 cc. per liter at 70°F.)

Organism		No Exposure		2 Hr. Exposure		4 Hr. Exposure	
		Growth		Growth		Growth	
		24 hr.	48 hr.	24 hr.	48 hr.	24 hr.	48 hr.
Alpha streptococcus	1	+	+	−	−	−	−
	2	+	+	−	−	−	−
Staph. aureus	3	+	+	+	+	−	−
	4	+	+	?	+	−	−
Escherichia coli	5	+	+	−	−	−	−
	6	+	+	−	−	−	−
Aerobacter aerogenes	7	+	+	−	−	−	−
	8	+	+	—	—	—	—
Ps. aeruginosa	9	?	+	−	−	−	−
	10	?	+	−	−	−	−
Proteus vulgaris	11	+	+	−	−	−	−
	12	+	+	−	−	−	−
Pneumococci	13	−	−	−	−	−	−
	14	+	+	+	+	−	−

workers immediately after they had been sterilized by ethylene oxide vapor. Apparently the vapor had dissolved in the rubber and diffused out against the skin. Plastics in general share this property of dissolving this gas. No such incidents have occurred with similar articles of clothing which were aired before being worn.

Sterilizing of Liquids with Ethylene Oxide

Use of ethylene oxide to sterilize liquids, including ophthalmic solutions, is impractical at the present. A sufficient amount of the liquid ethylene oxide must be added to a given solution to bring the concentration to one percent. The container is then stoppered and let stand for six hours or longer. After that time the solution must be exposed to air to allow the gas to evaporate. To hasten this process, the open container should be heated to 60°C., and a 25 pounds per square inch vacuum drawn for one minute.

Studies have not been carried out to determine if there is a chemical reaction between the ethylene oxide and the solution being sterilized. The medication cannot be used clinically until all the ethylene oxide has evaporated. Thus there is no continuing inhibition of contamination with micro-organisms. There is a pH change which must be moderated by various buffers. Dry streptomycin calcium chloride salt looses 35 percent of its potency when treated with ethylene oxide vapor. Penicillin in the dry powdered form showed no diminution of potency.[5] For sterilizing liquids, it is considerably more simple to employ either a Selas porcelain filter or a membrane filter.*

Summary

Ethylene oxide vapor is an effective sterilizing agent against both bacteria and at least the larger viruses. Packaged in a convenient 12-ounce can containing about 80 percent dichlorodifluoromethane, the ethylene oxide is easily admitted to an ordinary small steam sterilizer which requires only simple modifications for this purpose. A four-hour exposure to ethylene oxide vapor at room temperature killed all organisms tested. Toxicity is a negligible factor in the amounts used here. Bulky items and instruments which are harmed by heat or soaking can be rendered sterile with no damage whatsoever. Plastic, rubber, leather, electrical equipment, wood, and paper are not harmed by this method of sterilization with ethylene oxide vapor.

Walter Reed Army Hospital (12).

* Millipore Filter Company, Watertown, Massachusetts.

References

1. Phillips, C. R., and Kaye, Saul: The sterilizing action of gaseous ethylene oxide, I. Review, Am. J. Hyg., **50**:270-279, 1941.

2. Kaye, S., and Phillips, C. R.: The sterilizing action of gaseous ethylene oxide: IV. The effect of moisture. Am. J. Hyg., **50**:296-306, 1949.

3. King, J. H., Jr.: Contamination of eye medications: Practical methods of prevention. Am. J. Ophth., **36**:1389-1397, 1953.

4. Blackwood, J. D., and Erskine, E. B.: Carboxide poisoning. U. S. Naval Med. Bull., **36**:44-45, 1938.

5. Kaye, S., Irminger, H. F., and Phillips, C. R.: The sterilization of penicillin and streptomycin by ethylene oxide. J. Lab. & Clin. Med., **40**:67-72, 1952.

THE PHOSPHORUS METABOLISM IN THE LENS*

H. K. Müller, O. Kleifeld, H. P. Arens, U. Dardenne,
R. Fuchs, and O. Hockwin
Bonn, Germany

Importance of phosphate metabolism

Phosphate is of great importance to the metabolism of the cell. In its inorganic form the phosphate ion acts as an electrolyte in the maintenance of osmotic pressure. Since it is a tribasic acid, phosphoric acid is particularly helpful in keeping the hydrogen-ion concentration constant. Due to its ability to alter its degree of dissociation, it acts as a buffer. Phosphate is required as a reaction-partner for many fermentation processes. It is also an important basic material of such vitally necessary substances as, for instance, the phosphatides (lecithin, cephalin, sphingomyeline). In addition, it is an essential component of nucleic acids, that is to say, of the chromosomes and genes, which are those substances of the nucleus and cell-plasma essential to life. Mention must be made of the phospho-proteins. The phosphate ion plays a very important part as a component of vitamins and coferments as, for instance, codehydrogenase I and II, diaphorase, flavine, and co-carboxylase.

Phosphate plays a special part in the energy metabolism. It is the task of the phosphate metabolism to collect the energy gained from the catabolism of nutrients in phosphate compounds rich in energy, to store it, to transport it to the points required and make it available there. The collection of energy from reactions supplying energy is done in such a way that a phosphate group of a combination rich in energy is added to an organic substance.

We know of several forms of phosphate compounds rich in energy. The type most frequently encountered, as found also in adenosine triphosphate (ATP), is that of several phosphoric acids in an anhydride combination. Among other kinds of phosphate compounds rich in energy are the enol phosphates (for instance, phosphoenolpyruvic acid), the acyl phosphates (for instance, acetyl phosphate or phosphoglyceric acid), and the amidine phosphates, where phosphorus is combined with nitrogen (for example, creatine phosphate and arginine phosphate). Recently, another compound rich in energy, in which phosphate is combined with sulphur, has come to the fore more and more; this is found, for instance, in the coenzyme-A-phosphate.

ATP is the most important of the phosphates rich in energy. Even today, the manner in which it is formed may be classified under two headings:

In the first process the energy released from the catabolism of a substrate is used in order to convert the substrate itself into a phosphate compound rich in energy. After this so-called substrate-phosphorylation, this phosphate group is transphosphorylized to ADP, and ATP is formed. The second manner in which ATP is formed follows the process of the respiratory chain phosphorylation and is also called oxidative phosphorylation. In its case the energy released by the oxidative catabolism of a substrate is transmitted via numerous intermediate products. The exact manner in which this process is accomplished is, as yet, unknown.

If the energy gained from the exergonic reactions is not immediately required for endergonic cell activities, it can be stored in highly energized phosphate compounds. The phosphate residue is transphosphorylized to creatine in the process. If an increased demand for energy occurs anywhere in the metabolic process, this store of energy is tapped.

The importance of this collection and

* Presented at the International Symposium on Physiology and Pathology of the Eye, Iowa City, Iowa, September, 1954.

storage of energy lies above all in the fact that energy in utilizable form is made available to the cellular metabolism in this way. Energy is transferred to a substrate by the addition of a phosphate residue of ATP. It has thus become more reactive, since energy is released by the splitting off of this phosphate group, which renders possible the endergonic reaction of this substrate.

We know that phosphate plays the part described in the energy metabolism of the lens.

The lens requires an energy metabolism, since it is an organ composed of living cells. Vigorous metabolic processes are noticeable at least in the epithelial cells of the lens and in the superficial layers of the cortex. The cells multiply up to the most advanced age. The synthesis, transformation, and catabolism of protein, accompanied by the consumption of glucose, as well as of numerous other substances, is required for this purpose.

Simultaneously, the transparency of the lens must be guaranteed for the duration of life. This is possible only if a physicochemical state of balance is maintained. Energy is also required for this. The metabolism of the cells of the lens can—as is the case with the rest of the body's cells—be maintained only if a certain relationship between the potassium and sodium ions is preserved both intra- and extracellularly. These processes also require energy. We know furthermore, at least with regard to some substances, that their absorption by the lens, and their being given off to the aqueous humor, consumes energy.

A number of other examples of processes requiring energy could be cited, but for the moment we will dispense with these. I should merely like to draw attention to one more process, where we assume that energy is required. It is that of Kleifeld's (1953 a and b) more detailed investigation of the subject of active participation of the lens fiber in accommodation.

The investigations of Kinsey and Merriam (1950) point to the importance of ATP for the protein synthesis of the lens. When making tests with radioactive-labelled glycocoll they found, at those points of the lens which displayed a high content of ATP, a considerably more speedy rate in the protein acceptance than in places of low ATP content.

Mishima (1952) demonstrated that vitamin-C production by rat lenses from mannose can be increased by the addition of ATP. H. K. Müller had already demonstrated in 1937(a) that the lens becomes impoverished of vitamin C after phlorizin poisoning, which hampers the process of phosphorylation.

The energy required for all these processes is produced by the cells of the lens to an even greater degree than by the remaining cells of the body, chiefly through the aerobic and anaerobic carbohydrate catabolism.

What we know of the phosphate metabolism of the lens

It may be gathered from the introductory sentences on the general importance of the phosphate metabolism that phosphate plays a very important part in the energy economy of the cell. In this connection we may speak of an intracellular phosphate circulation. The inorganic phosphate is synthesized in the course of energy-producing catabolic processes into organic phosphate compounds rich in energy, and catabolized once more into inorganic phosphate when cellular activity requires energy.

The carbohydrate metabolism is particularly closely linked with this phosphate metabolism for two reasons. The manner in which carbohydrate catabolism takes place in its anaerobic sector, that is, that of glycolysis, is possible only via phosphorylized intermediary products. In addition, the energy required for the synthesis of phosphate compounds rich in energy is for the major part gained from carbohydrate catabolism. The latter applies to the lens particularly, since the catabolism of fats ap-

pears to play a lesser part here than it does in comparison with the rest of the organism.

The principal cause of disturbances and slowing down of the metabolism, such as we find in the occurrence of cataract and when the lens ages, is therefore likely to be found in disturbances of the carbohydrate metabolism. Nordmann (1954) has pointed this out particularly forcefully.

In consequence of the above-mentioned close relationship between the carbohydrate metabolism and the phosphate metabolism of the lens, disturbances of the carbohydrate metabolism must lead to corresponding changes in the phosphate metabolism. It would appear appropriate for these reasons to discuss the phosphate metabolism in the chronologic order of carbohydrate catabolism.

1. Glycogenolysis

Several authors agreed that lens extract is capable of catabolizing glycogen (Süllmann, 1937a, Weekers and Süllmann, 1938, Leinfelder and Christiansen, 1952). In this connection the catabolism of glycogen into lactic acid is alleged to be combined with a greater consumption of inorganic phosphate than the catabolism of glucose (Weekers and Süllmann, 1938). Since, according to Lo Cascio (1922), no amylase is said to occur in the lens, which would split the glycogen by the direct hydrolytic method, the authors assume that the glycogen is split by the lens extract with the aid of phosphorylase. This catabolism of glycogen generally takes place via glucose-1-phosphate according to Figure 1.

In fact, Nordmann and Mandel did prove the presence of this phosphoric acid ester in the lens in 1952. For the time being the importance of the ability of the lens tissue to catabolize glycogen phosphorylytically is obscure. For the formation of lactic acid from glycogen is not possible in an intact lens, since the capsule is impenetrable to glycogen (Leber, 1906, and Süllmann, 1937a).

The presence of glucose-1-phosphate might be due to the fact that the lens is in a position to synthesize at least part of the glucose absorbed via glucose-1-phosphate into glycogen. But it appears that Leber failed in 1906 in his attempt to prove the presence of glycogen in the lens. Nor were Weekers and Süllmann able to find it in 1938, either in the lens of adult cattle or calves.

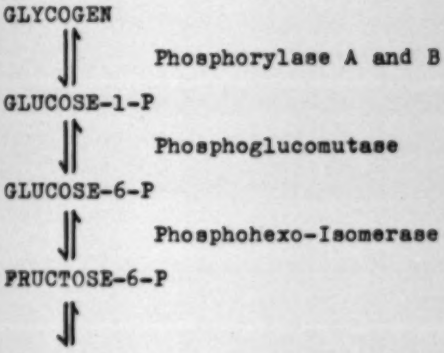


Fig. 1 (Müller, et al.). Catabolism of glycogen.

It is not known whether there is a subsidiary way for glycolysis in the lens, which might lead via glucose-1-phosphate. It might also be possible that some other substance in the lens can be synthesized or catabolized via glucose-1-phosphate. Inosite, which is catabolized via adenylic acid, might, for instance, be considered. It occurs in the lens in a comparatively high concentration (Schmid and Bürki, 1943). Despite this, hardly anything is known of its function in the lens (Krause and Weekers, 1938). Boyland assumed in 1928 that inositol could be converted in the cell both into glycogen and glucose. Stetten and Stetten were able to demonstrate, in 1946, that mesoinositol can be transformed into glucose, though only to a very small degree.

If glucose-1-phosphate in the lens were an intermediary product of the synthesis or catabolism of glycogen, then glucose-1,6-diphosphate would also have to be present in the lens. For this phosphatic ester is the coenzyme of phosphoglucomutase, the enzyme

which catalyzes the rearrangement of glucose-1-phosphate into glucose-6-phosphate. Hitherto the available literature provided no information on the presence of this enzyme in the lens.

The most common line of glucose catabolism therefore does not in the lens, in all probability—contrary to that of the muscle—take place via glycogen. It would appear, rather, that the glucose absorbed from the aqueous humor is catabolized directly.

2. Glycolysis

The first step to glycolysis is the addition of phosphate to glucose with the aid of the enzyme hexokinase. The necessary phosphate residue is split off ATP. This results in glucose-6-phosphate. In 1938, Weekers and Süllmann were able to activate the formation of lactic acid in the lens vigorously by the addition of phosphate as well as hexokinase. The fact that glucose, mannose, and fructose are equally utilizable for glycolytic catabolism in the lens (Süllmann, 1937a, Leinfelder and Christiansen, 1952, Ross, 1953) points to the likelihood that this phosphorylation is achieved by the unspecific hexokinase. It is not known whether the specific glucokinase and fructokinase occurring in muscles and in the liver exist also in the lens. Achard (1954) obtained metabolic disturbances by means of inhibiting substances from hexokinase, such as iodine monoacetic, and phloridzin, which showed in a reduced ATP content and accompanying clouding of the lens.

This hexokinase enzyme appears to play a part when glucose is resorbed from the aqueous humor (Nordmann, 1954). Though the hexose can penetrate the lens capsule (Nordmann, 1954, Friedenwald, 1930) several research scientists were able to demonstrate that glucose resorption in the lens is connected with an active metabolic process. Müller (1939) was able to obtain a strong inhibition of glucose resorption by adding iodine monoacetic acid to the nutrient solution. On the other hand, Ross (1953) was able to obtain a noticeable increase of hexose-resorption by adding insulin to the surrounding glucose solution.

The powers of inhibition by means of iodine monoacetic acid and in all probability of activation by means of insulin are properties of animal hexokinase (Walaas and Walaas, 1952, Chernick, Chaikoff, and Abraham, 1951, and others). Hexokinase in the lens was measured by van Heyningen and Pirie (1953) and examined by Nordmann (1954), and Weekers and Süllmann in 1938.

According to the latest research work by Dische and his collaborators (1953) the entire lens capsule has a high ATP content and an active metabolism. Frohmann and Kinsey (1952) were also able to demonstrate the presence of ATP in the anterior and posterior lens capsule. The conclusion may be drawn from all these studies that resorption of glucose may possibly go hand in hand with a fermentative phosphorylation by means of the hexokinase enzyme and of ATP as the supplier of phosphate (Nordmann, 1954). The phosphate residue can be split off again after passage through the capsule, so that glucose may be partially present in the lens in its free form. The phosphatases required for this purpose have been found by many research scientists in the lens (Müller, 1937b, Süllmann, 1937a, Santoni, 1938, Brolin and Nordström, 1952, Pignalosa, 1939a, Zimmer, Mandel, and Nordmann, 1952). This dephosphorylation probably takes place in part in the capsule. The presence of phosphatases has been proved here as well (François and Rabaey, 1951).

In order to be further catabolized the dephosphorylized glucose must be phosphorylized once more. The phosphorylizing power of the lens was proven (Müller, 1937b, Süllman, 1937a, Weekers and Süllmann, 1938, Pignalosa, 1939a, Milano, 1941, Palm, 1948).

Süllmann (1937a) discovered that the lens can catabolize galactose to lactic acid, though only to a limited degree. This was confirmed

in 1952 by Leinfelder and Christiansen, and in 1953 by Ross. According to Weekers (1941), this is hardly of any importance in a normal lens, but the fundamental ability of adopting this method of catabolism remains undisputed.

If we assume that glycolytic catabolism takes place in the lens in essentially the same manner as in most of the other body cells, then the catabolism of galactose would require the presence of an additional phosphate-transferring system of enzymes in the lens. We know that the organism first of all phosphorylizes galactose into galactose-1-phosphate by galactokinase. This phosphate ester is rearranged into glucose-1-phosphate by galactowaldenase whose co-ferment is uridine diphosphate glucose. Catabolism is then effected in the usual way after mutation into glucose-6-phosphate.

Though the importance to be attributed to subsidiary ways of glucose in the lens—to be further discussed later—has not yet been fully clarified, the principal process would appear to be the same as in the rest of the organism (fig. 2). Glucose-6-phosphate is first of all rearranged by phospho-hexose-isomerase into fructose-6-phosphate. The occurrence of this enzyme in the lens does not appear to have been specially investigated hitherto.

ATP now intervenes for the second time in the catabolism of glucose. It transfers a further phosphate residue to the fructose-6-phosphate. That is how fructose-1, 6-diphosphate occurs. This process is also steered by a specific enzyme, namely, phosphofructokinase. The existence of this enzyme was proved by Mandel and Israelewicz in 1953. Müller (1937b) was the first to investigate the subsequent splitting of fructose-1, 6-diphosphate (Harden-Young-ester) into the two triosephosphates, dioxyacetone phosphate and glyceraldehyde phosphate, in the lens. Mandel and Israelewicz (1953) were able to demonstrate the aldolase required for this purpose by means of purified lens extracts. The adjustment of balance between dioxy-

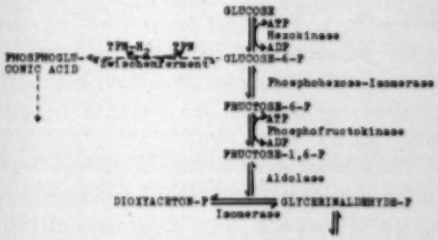


Fig. 2 (Müller, et al.). Glycolysis, Part I.

acetone phosphate and glyceraldehyde phosphate by means of isomerase has not as yet been examined in detail in the lens. Süllmann (1937) was able to inhibit glycolysis in the lens by the addition of glyceraldehyde, the inhibiting effect of which on aldolase is known.

The phosphorylation processes of glucose catabolism hitherto discussed required energy. For the purpose of gaining this energy, therefore, the phosphate group to be added had to be split off an organic phosphate compound rich in energy. As is the case everywhere else in the organism, the lens also makes use of ATP for this purpose. But with regard to the reaction which follows, the energy released due to dehydrogenation is used in order to add an inorganic phosphate residue to the substrate. The 3-phosphoglyceraldehyde is dehydrogenated and at the same time phosphorylized into 1,3-diphospho-glyceric acid. This compound is an acyl phosphate and is on a higher energy-level than ATP. The enzyme which catalyzes this reaction is the triosephosphate-dehydrogenase with the coenzyme diphospho-pyridine nucleotide (DPN). Iodine monoacetic acid is specific inhibitor of this enzyme.

Achard (1954) achieved the already mentioned reduction of ATP-content and clouding of the lens by adding this inhibiting substance. Mandel and Israelewicz (1953) were also able to demonstrate this glycolysis stage in the lens in the course of their latest experiments. The acyl phosphate group was split by the so-called first dephosphorylizing ferment. It is transferred to ADP by transphosphorylase. The glycolytic balance

of energy is now level again, since the two ATP molecules which were used up in forming fructose diphosphate have been synthesized again from one molecule of glucose (fig. 3).

The catabolism of 3-phospho-glyceric acid, in the manner known hitherto, would require a transformation into 2-phospho-glyceric acid. The enolase would split one molecule of water off this compound and phospho-enol-pyruvic acid would be created. This splitting off of water would be a gain in energy for the cell, since the enolic phosphate combination now available is rich in energy.

The second dephosphorylizing enzyme splits off the phosphate group. The energy released is collected by transfer of the phosphate residue to ADP accompanied by the formation of ATP. One molecule each of ATP is in turn gained in this manner from the two trioses of the glucose molecule. These two ATP molecules represent the actual gain in energy of glycolysis.

Until recently the course taken by this energy-producing partial reaction of glycolysis could be proved only indirectly in the lens. It is known that enolase can be specifically inhibited by means of sodium fluoride (NaF). Several authors (Müller, 1937a, Weekers, 1940, Achard, 1954) were able to inhibit the formation of lactic acid

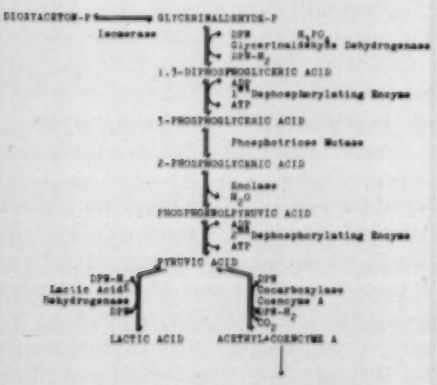


Fig. 3 (Müller, et al.). Glycolysis, Part II.

and in part also the formation of ATP by adding sodium fluoride to the nutrient solution. This made it probable that enolase participated in the glycolysis of the lens.

Krause, 1938, Weekers, 1940, Fischer, 1947, Kinsey and Frohmann, 1951, Mandel and Zimmer, 1952, and Auricchio and Ambrosio, 1953, were able to prove in addition the presence of pyruvic acid in the lens. In 1953, van Heyningen and Pirie stated that they had proved the presence of all enzymes which cause the glycolytic catabolism of glucose in the usual manner elsewhere in the organism in the lens as well. Evidence of lactic-acid dehydrogenase thus also provides proof of the last step of glycolysis, namely, the possibility of converting pyruvic acid into lactic acid.

The importance of phosphate to the glycolytic share in the glucose catabolism of the lens may be summarized as follows:

The energy released by the catabolism of one molecule of glucose to two molecules of lactic acid is collected in four phosphate compounds which are rich in energy. Two of these are required in order to phosphorylize a new glucose molecule and to make this accessible to the same catabolism. The two remaining molecules of ATP are available to the lens in a utilizable form for any processes that may require energy. The potential energy of two ATP molecules is about 24,000 calories. This yield is comparatively small if one considers that about 450,000 calories are gained from the complete oxidative catabolism of glucose.

3. The oxidative catabolism of carbohydrate

The oxidative catabolism of carbohydrates is almost always initiated by a catabolism of the glucose molecules in the manner already described down to pyruvic acid. The following difference is apparent between this first part of the oxidative catabolism as compared with glycolytic catabolism as far as lactic acid:

The H-ions split off during dehydrogena-

tion of glyceraldehyde phosphate are not transferred to pyruvic acid for forming lactic acid. On the contrary, the reduced codehydrase transfers its two H-atoms to the respiratory chain system. Three ATP molecules are thereby synthesized. So this part of the process already produces an additional gain of three ATP molecules as compared with the purely glycolytic catabolism. Despite the fact that subsidiary ways of glycolytic and oxidative glucose catabolism have repeatedly been discussed and discovered particularly in the case of the lens, we will first of all discuss the usual oxidation mechanism of pyruvic acid via the so-called citric-acid cycle.

a. *The citric-acid cycle* (fig. 4)

The citric-acid cycle represents the broad road of the entire nutrient catabolism, and the catabolic paths taken by the carbohydrate metabolism, the protein metabolism, and the fat metabolism join it. This path passes over nine intermediary products, and their decarboxylations and dehydrogenations when catabolizing one molecule of pyruvic acid produces 15 molecules of ATP.

We will demonstrate the course taken by this catabolic process by the use of this simple diagram and, following this, we will discuss its important relationship to the phosphate metabolism. In this connection we

Fig. 4 (Müller, et al.). The citric-acid cycle.

are deliberately dispensing with an exact description of the individual reactions.

The pyruvic acid is oxidatively decarboxylized with the aid of cocarboxylase, DPN, and the coenzyme-A, and condensed as "activated acetic acid" by the "condensing enzyme" with oxalacetic acid to citric acid. The aconitase dehydrates the citric acid to cis-aconitic acid and then adds the water again in such a manner that the hydroxyl-group is placed next to another C-atom, accompanied by the formation of isocitric acid. According to the latest research, cis-aconitic acid itself is not created, but an intermediate product which is easily stabilized as cis-aconitic acid. In the presence of manganese^{++} or magnesium^{++} the isocytricodehydrase together with TPN as a coferment dehydrogenates the isocitric acid into oxal-succinic acid. Iodoacetate and fluoroacetate inhibit this ferment.

A rigidly specific decarboxylase will now split CO_2 off oxal-succinic acid in the presence of bivalent metal ions, and produce α-ketoglutaric acid. The releases 4,460 calories.

In the same way as with pyruvic acid, an oxidative decarboxylation of α-ketoglutaric acid into succinic acid will now follow in the presence of DPN, cocarboxylase, and coenzyme-A.

Succinic acid is dehydrogenated into fumaric acid by succinodehydrase. This reaction requires about 20,000 calories and can be inhibited by malonic acid. Fumaric acid is hydrated by fumarase into malic acid. This ferment is very sensitive to heavy metals and probably works without a coferment. Malic acid is dehydrogenated into oxalacetic acid. This closes the cycle, as it is again condensed into citric acid with the activated acetic acid.

It was considered doubtful for a long time as to whether the citric-acid cycle progressed in the lens in the manner described above. Even though it was possible to prove the presence of the individual intermediary products of the citric-acid cycle (Krause,

1938, Krause and Stack, 1939, Ely, 1951), it was found impossible for a long time to demonstrate singly the ferments required for this purpose. Lodato made the first unsuccessful attempt in 1906 to prove the presence of oxadases in the lens. In 1927, Ahlgren showed that the lens is in a position to oxidize pyruvic acid, citric acid, fumaric acid, and malonic acid, but not succinic acid. Adams (1925) had obtained the same results, but was able to prove in addition that the succinic acids could be oxidized in the lens as well by the aid of succinodehydrase. Ely confirmed this result in 1951, and expanded it to the effect that oxalacetic acid and α-ketoglutaric acid are also oxidized. Mandel and Klethi (1954) were also able to confirm the presence of succinodehydrase in the lens beyond any doubt.

All the catabolic steps of the citric-acid cycle had thus been proven in the lens, and it may therefore be assumed with reasonable certainty that the citric-acid cycle progresses in the lens also in the manner already described. Nordmann (1954) also supports this opinion, since all the ferments required are present in the lens. Achard's work (1954) provides an important result. He discovered that malonate and fluoroacetic acid, which are known to inhibt the citric-acid cycle, cause a notable reduction in ATP. So we may further assume that the lens makes use of oxidative nutrient catabolism through the citric-acid cycle in order to synthesize phosphate compounds rich in energy. The P:O quotients of the individual catabolic steps, that is, the amount of phosphate rich in energy per quantity of oxygen accepted, have been fully investigated in the lens. But the P:O quotient is of decisive importance for the question of which systems are used for the transport of H-ions in the lens. A more detailed discussion of this problem will follow.

b. *The phosphate metabolism within the citric-acid cycle*

As already mentioned briefly in the introduction, one can differentiate in principle between two different ways of obtaining energy from nutrient catabolism: by substrate phosphorylation and by oxidative phosphorylation. In the case of glycolysis, substrate phosphorylation occurred in such a manner that the phosphate residue was combined with the reacting substance itself. A substrate phosphorylation is to be found also in the citric-acid cycle, but only an indirect one (Lynen and Holzer, 1949, Felix, 1953). For when there are two oxidative decarboxylations, phosphate is temporarily added to coenzyme-A and is only transferred by this to ADP. By far the greater part of the phosphate compounds rich in energy which are synthesized by the citric-acid cycle are, however, formed by oxidative phosphorylation. By this I mean the formation of ATP, which takes place during the stepwise decrease of energy when the H_2 molecules are being brought to the oxygen. This formation of ATP occurs within the respiratory chains which start at five different places in the citric-acid cycle.

The oxydative decarboxylation of pyruvic acid and the transition to the citric-acid cycle have been the subject of numerous investigations during the last few years. The discovery of "activated acetic acid" by Lynen and his collaborators (1951a and b) has substantially cleared up the mechanism of this process and also the transition of the fatty acid catabolism into the citric-acid cycle. Though these investigations have not yet been carried out in detail with regard to the lens, we may assume, as demonstrated above, that the transition from glycolysis to the citric-acid cycle is possible in it in the same way.

Hardly any investigations have been made regarding the fatty acid catabolism in the lens. But in consequence of the high content of the lens in lipoids, and the occurrence of neutral fats and free fatty acids (Krause, 1934, 1935), these processes, too, are to a certain extent of importance for the lens. De Leonibus (1941) and Pignalosa (1944) were able to demonstrate that the catabolism of fatty acids in the lens is effected via β-oxidation and that the discharging into the

citric-acid cycle of the acetic acid residue which has formed takes place in just the same way as in the rest of the body.

It would introduce unnecessary complications at this point to go into the multitude of details and problems as yet unsolved which this important section of the citric-acid cycle presents. The extraordinary importance of the phosphate metabolism as regards these reactions will also become obvious if we discuss these processes in a simplified form just as in all probability they take place in the lens.

The coenzyme-A, a co-ferment consisting of adenosine-5-phosphate, two further phosphate groups, pantothenic acid and probably ethyl-aminothiol, is added to the keto-group of pyruvic acid together with the terminal SH group. The dehydrogenation by DPN and decarboxylation through aneurinpyrophosphate (cocarboxylase), already mentioned, takes place in this state (fig. 5).

The coenzyme-A-acetate compound thus created is the so-called "activated acetic acid," a compound rich in energy. By means of the condensing enzyme this acetate condenses with oxalacetic acid into citric acid. It is probable that all other acetylation processes in the animal organism also takes place via this "activated acetic acid."

It was thought for some time that a so-called "phosphoryclastic" split existed in addition to this so-called "thioclastic" split of pyruvic acid with coenzyme-A. Instead of coenzyme-A, a phosphate residue was supposed to be added thereby to the keto group of pyruvic acid. Oxidative decarboxylation was then supposed to follow in this state. Acetyl phosphate was then supposed to be the final product. But hitherto this acetyl phosphate has been demonstrated only

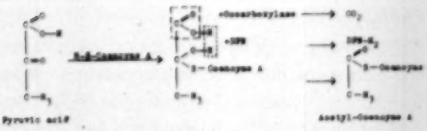


Fig. 5 (Müller, et al.). The oxidative decarboxylation of pyruvic acid.

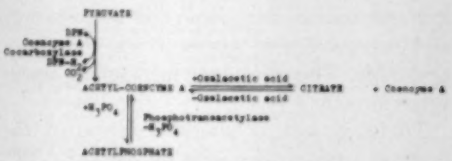


Fig. 6 (Müller, et al.). The formation of acetylphosphate and citrate from Coenzyme A.

during catabolism of pyruvic acid by bacteria. According to investigations conducted during the last few years, however, this second process of pyruvic catabolism, in which the phosphate metabolism intervenes, cannot be fundamentally different from the one first described. The formation of acetyl phosphate in all likelihood follows a by-path according to Figure 6.

It therefore acts merely as a storehouse both for the activated acetate and for the phosphate rich in energy, since its phosphate can be transferred to ADP. The presence of phosphotransacetylase is required for its formation. The occurrence of this enzyme in animal tissue has not yet been proved. The lens does not appear to have been examined yet in this respect. On the other hand, a highly effective acetyl phosphatase occurs in animal tissue, which will immediately split acetyl phosphate, which has formed. It is not known whether the lens possesses the ability to do the same.

A further enzyme—formo-transacetylase—was found in bacteria. In the presence of this enzyme, pyruvic acid can be catabolized to acetyl-coenzyme-A in anaerobic surroundings as well. The pyruvic acid, which may also be regarded—from the chemical aspect—as acetyl-formic acid, is split into acetate and formic acid. It is not known to me whether this enzyme has in the meantime also been found in animal tissue. In view of the fact that a large part of the lens metabolism is anaerobic, it would make possible the catabolism of pyruvic acid into activated acetic without the consumption of oxygen.

As already mentioned, the acetate residues that split off during the fatty-acid oxidation

are also activated by means of coenzyme-A and incorporated in this shape into the citric-acid cycle. The phosphate metabolism intervenes directly here.

To begin with, a phosphorylation of coenzyme-A takes place with the help of ATP. An exchange of its phosphate against acetate takes place, and coenzyme-A-acetate is formed. Here, too, the additional enzyme has been found in bacteria, which enzyme assembles acetate and phosphate into a combination rich in energy. It is, therefore, the task of this phosphotransacetylase to do the following:

According to the quantity of catabolized pyruvic acid or of acetic acid residue available and the requirements of activated acetate, it must store the latter in a form rich in energy, or mobilize it rapidly. The phosphotransacetylase only effects a shift of the acetate between coenzyme-A and phosphate, always on the same high level of energy. A direct transfer of ATP-phosphate to acetate, as was formerly thought to take place, is impossible for thermodynamic reasons alone, since the acyl phosphates are richer in energy than the pyrophosphates.

When pyruvic acid is catabolized to acetic acid, four molecules of ATP are gained—three of them by way of respiratory chain phosphorylation during the electron-transport of the H-ions transferred to DPN during dehydrogenation, and one by substrate-phosphorylation of coenzyme-A. It is supposed that the latter takes place in such a way that the acetate which is combined with coenzyme-A is exchanged against a phosphate residue. The coenzyme-A-phosphate thus formed transfers the phosphate to ADP. This gaining of energy via the phosphorylation of coenzyme-A is not, however, possible in the progress of the citric-acid cycle, since the energy of the coenzyme-A-acetate combination is used for the condensation of the acetate with oxalacetic acid. It is therefore preserved to the system of the citric-acid cycle and is only released after further catabolism. The energy gained by this first step therefore amounts to three molecules of ATP.

The following conversions of citric acid into isocitric acid appear to take place without reference to the phosphate metabolism:

The dehydrogenation of isocitric acid into oxal-succinic acid supplies three molecules of ATP by way of the respiratory chain. The phosphorylation processes within this action will be referred to once more in greater detail.

The decarboxylation of oxal-succinic acid into α-ketoglutaric acid takes place without the intervention of the phosphate metabolism.

According to recent experimental investigations, the catabolism of α-keto-glutaric acid into succinic acid has a P:O quotient of 4, so that four molecules of ATP are synthesized for every molecule of oxygen absorbed. But after addition of dinitrophenol (DNP) only one molecule of ATP was synthesized. This was experimental confirmation of the view that the catabolism of α-keto-glutaric acid takes place in a manner similar to that of pyruvic acid. For since dinitrophenol separates the respiratory process from the phosphorylations thereto appertaining, the three ATP molecules gained by the oxidative decarboxylation of α-ketoglutaric acid through dehydrogenation cannot be synthesized anymore. Only that energy can still be trapped at ATP which has been gained via the substrate-phosphorylation of coenzyme-A. The process takes place in the following manner: The SH-group of coenzyme-A is added to the keto-group of α-ketoglutaric acid. The dehydrogenation by DPN and the decarboxylation to succinyl-coenzyme-A then takes place. The residue of succinyl is exchanged against a residue of phosphate, and this is then transferred to ADP.

In the case of dehydrogenation of succinic acid into fumaric acid, the oxidative phosphorylation produces a yield of only two ATP molecules. The reason is that the H-ions are conveyed to the oxygen by another

way than that taken after the dehydrogenation of the other substrates. This way contains only two steps where the energy released suffices to add inorganic phosphate to ADP.

The hydration of fumarate into malate by fumarase takes place without contact with the phosphate metabolism. Malic acid is dehydrogenated into oxalacetic acid, and thereby three molecules of ATP are gained in the usual way via oxidative phosphorylation.

Thus, when the citric-acid cycle progresses normally a total of 15 molecules of ATP are synthesized.

Figure 7 shows a compilation of the individual reactions of oxidative catabolism of a molecule of glucose, whereby ATP is synthesized.

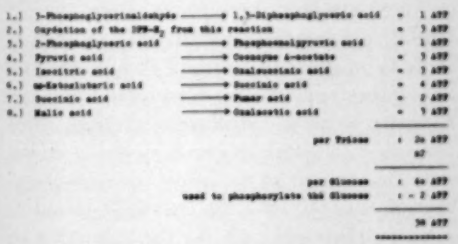

1.) 3-Phosphoglycerinaldehyde → 1,3-Diphosphoglyceric acid = 1 ATP
2.) Oxydation of the DPN-H_2 from this reaction = 3 ATP
3.) 2-Phosphoglyceric acid → Phosphoenolpyruvic acid = 1 ATP
4.) Pyruvic acid → Coenzyme A-acetate = 3 ATP
5.) Isocitric acid → Oxalacetate acid = 3 ATP
6.) α-Ketoglutaric acid → Succinic acid = 4 ATP
7.) Succinic acid → Fumar acid = 2 ATP
8.) Malic acid → Oxalacetic acid = 3 ATP
per Triose : 2x 15 ATP
30
per Glucose : 4x 30 ATP
used to phosphorylate the Glucose : - 2 ATP
38 ATP

Fig. 7 (Müller, et al.). Summary of the possible phosphorylations during the oxidation of one glucose molecule.

This computation is the result of theoretic considerations based on experimental findings, during which the individual stages of the citric-acid cycle were investigated by themselves. This figure therefore represents the optimum gain of energy. The processes are naturally far more complicated within the cell itself. This is because a series of reactions intervene in this cycle, which will be referred to in more detail owing to their close relationship with the phosphate metabolism. It is a further essential prerequisite for obtaining the yield of energy already mentioned that the respiratory chain should progress via the cytochrome system.

We will therefore discuss this mechanism first and, at the same time, examine to what extent the same conditions may be supposed to exist in the lens as have hitherto been found in the rest of the organism.

c. *The respiratory chain phosphorylation*

After the dehydrogenation of the substrates by the individual dehydrogenases, the hydrogen itself is first of all transported toward the oxygen by the hydrogen transfer enzymes. The coenzymes DPN and TPN, both with the active group nicotinamide, then receive the hydrogen and transfer it to the flavin enzymes. These substances contain their energy in a reduced state, combined with a material carrier, namely, the H-ions. They can, therefore, serve for the transport of energy in the same way as ATP. But following upon them, energy is transmitted within the Warburg-Keilin-system only by conduction, that is, only electrons are transmitted within the cytochrome system, the active group of which is iron. The matter of the H_2-molecule remains stationary. The enzymes of the cytochrome system are firmly linked with the cell structure, that is to say, with the mitochondria. After the stepwise reduction of the potential energy of the H-ions within the cytochrome system, they react together with the oxygen, accompanied by the formation of water. Figure 8 reproduces the knowledge we have hitherto acquired in this field.

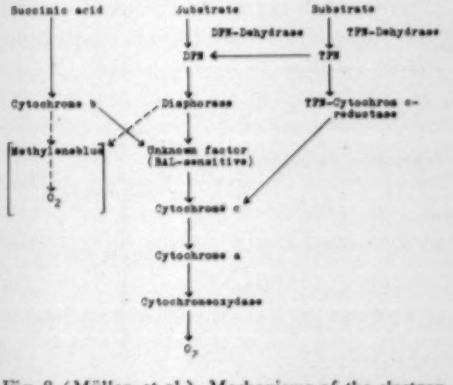


Fig. 8 (Müller, et al.). Mechanisms of the electron transport chain by Lang (1952).

There are only three places where the potential difference between the individual steps is so great that an ATP molecule can be synthesized: during transition from the flavine enzyme to cytochrome C, from cytochrome A to cytochromoxidase, and from the latter to oxygen. In the case of dehydrogenation of succinic acid, the energy is raised to a level sufficiently high for the formation of only one molecule of ATP during the last two steps.

Cellular respiration can be separated from the phosphorylation appertaining thereto by various substances, for example, by dinitrophenol (DNP), arsenious acid, sodium acid, methylene blue, and by a series of antibiotics, such as aureomycin and chloramphenicol. Large doses of thyroxin will also uncouple phosphorylation from respiration, whilst small doses will further it. If there is a lack of vitamin E and vitamin K_1, phosphorylation is also suspended without affecting respiration itself.

Martius (1954) developed a theory according to which the respiratory chain progresses in the way hitherto assumed only in the rare cases where no phosphorylation is linked with the respiration. The path most frequently followed he averred to lead via intermediary stages, which must be interpolated between those so far known, or else via bypaths approximately along the lines shown in Figure 9.

Martius believes he has proof of two of these additional H-ion carriers, during the dehydrogenation of which phosphorylation

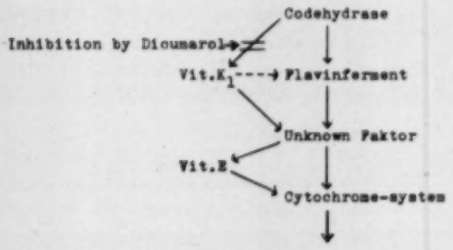


Fig. 9 (Müller, et al.). Mechanisms in the electron transport chain by Martius (1954).

is alleged to occur. They are vitamin K_1, which is interpolated between the codehydrases and the flavine enzyme or Factor X, and vitamin E between Factor X and cytochrome A. These substances can be replaced by other naphthoquinones. According to his investigations, these additional hydrogen transferring agents are eliminated by thyroxin, dinitrophenol, and dicumarol, and the direct path hitherto assumed is followed without the interpolation of these substances. Thus he explains that due to the influence of these substances the transfer of hydrogen released by hydrogenation does still occur, but that the energy gained thereby is not transferred to ADP, but is lost in the form of heat. But the precise phosphorylation processes within the respiratory chain are still unknown. It is probable that a phosphatic compound rich in energy, which is still unknown, is first of all synthesized by means of the energy obtained, and that this compound then transfers the phosphate to ADP, accompanied by the formation of ATP.

Numerous authors have considered the question of whether the respiratory chain system described exists in the lens. Euler and his collaborators proved the presence of the codehydrases I and II in the lens in 1938. For cattle lenses they discovered codehydrase I values of between 18.5 and 20.5 mg. percent fresh weight. The codehydrase II values were slightly lower, at 2.3 mg. percent fresh weight.

Proof of the occurrence of these coenzymes in the lens may also be found by reference to papers in which only the active group of these nucleotides, namely, nicotinamide, has been investigated. This nicotinamide is a product of the catabolism of codehydrases, and is created by the action of pyridine nucleotidases.

Corrado (1950) discovered diphosphopyridine-nucleotidase in the lenes of cattle. Euler and his collaborators (1939) discovered a nicotinamide content of 12.0 mg. percent fresh weight in the lens of cattle.

Kodicek (1940) states that cattle lenses contain 5.0 mg. percent of nicotinamide when fresh weighed. On the other hand, Simonelli (1941) found only 0.53 mg. percent, Cristini and Cuisa (1947) 1.6 mg. percent, and Fischer (1947) 8.2 mg. percent. These figures refer in each case to the fresh weight of cattle lenses. Fischer discovered a fresh-weight content of 17.6 mg. percent in the human lens.

Codehydrase I transfers its hydrogen to diaphorase, which is a flavine enzyme. According to Fischer (1936), the presence of the flavines in the lens can be proved. Giörgy (1935), Rochat (1939) and, above all, Euler (1938), disputed these findings. Philpot and Pirie were able to demonstrate the presence of riboflavin in ox lenses in 1943. The argument was settled by Kaganiya (1951) and by Kinsey and Frohman (1951). The former discovered a flavin content of 0.77 mg. percent in the human lens. Kinsey and Frohman proved the presence of riboflavin both in the epithelium and in the cortex. There was either very little in the nucleus or else none at all.

The available literature does not say whether the lens was examined with regard to the unknown factor, sensitive to BAL, whose presence is required by the rest of the organism when hydrogen is being transferred by diaphorase to the Warburg-Keilin system. But Herrmann and Moses, and Kinsey and Frohman were able to prove the presence of the cytochrome-cytochromoxidase-system in the lens in 1945 and 1951 respectively.

The investigations of Ely and Robbie (1950) show that this system intervenes in the internal cellular respiration of the lens. Since the cytochromes are hemin proteids and contain heavy metals, they can be inhibited with cyanide. These authors found that an addition of cyanide caused a 91 percent reduction of oxygen consumption.

Kronfeld and Bothman (1928) obtained a 10 to 40 percent increase in glucose-consumption by the use of cyanide. This effectiveness of the cytochrome system proves the presence of Factor X, if this is considered an essential prerequisite for the transfer of hydrogen to the cytochrome system. Since the presence of the individual links as well as the ferments of the oxidative catabolism of the lens could be proved, it would appear justifiable to assume that the lens is basically in a position to catabolize glucose into CO_2 and H_2O in a manner similar to that assumed in respect to the rest of the organism.

The extraordinary high incidence of redox systems of other kinds, such as glutathione, cysteine, cystine, and ascorbic acid, may be of great importance, due to their possible transverse connections with the cytochrome system. For, both glutathione and ascorbic acid can react directly with the cytochrome system. They might take the place of dehydrases and flavine ferments in this way.

It is further conceivable that the great number of redox systems present in the lens might function as an additional system for the transport of energy in the lens, in a manner similar to that of the codehydrases and flavine ferments in the rest of the organism. The majority of authors interpret these redox systems as a redox reserve for the cytochrome system.

The important question, which arose from the experiments of Christiansen and Leinfelder (1952), as to whether nonenzymatic respiration is possible in the lens and in what way this might take place, requires further investigation. But it would be more interesting from the aspect of the phosphate metabolism to find out how much energy would be yielded by such a possible nonenzymatic respiratory chain system. Unfortunately, no investigations appear to have been made on the subject as yet.

4. Phosphate metabolism in bypaths of nutrient catabolism

There are a series of reactions in addition to the catabolic processes already discussed,

which we have divided into an anaerobic and an aerobic phase, which obliterate these rigid differences. These bypaths have also been partially examined in the lens, and their presence has been plainly proved.

a. *The hexose-monophosphate shunt*

The oxidative catabolism of phosphorylized glucose via phosphogluconic acid should be mentioned first. Though this path is of only secondary importance for the gaining of energy, it does lead to ribophosphoric acid, which is of such importance for the synthesis of the majority of ferments.

The glucose-6-phosphoric acid is dehydrogenated by the codehydrase II by means of Warburg's "Zwischenferment," thus giving rise to phosphogluconic acid. Decarboxylation then gives rise to ribose-5-phosphoric acid. Since, contrary to what might have been expected, Arabinose-5-phosphate is not formed, a previous transference of the OH-group to C_3 must have occurred. As a result ribulose-5-phosphate is formed and out of this there is formed, in turn, ribose-5-phosphate. This process can be experimentally demonstrated in the organism. We may assume this process to apply also to the lens. Nordmann (1954) observed the occurrence of a C_5 sugar, when he allowed lens preparations to act on glucose-6-phosphate in the presence of codehydrase II. The transformation of the glucose-6-phosphoric acid into ribose-5-phosphate takes place without the presence of ATP and inorganic phosphate, and is in no way affected by iodomonoacetic acid and sodium fluoride. Ribose-5-phosphate is split up into a triose-phosphate and a C_2 fragment. This latter can be included in an oxidation mechanism such as the citric-acid cycle. The trioses become added together to form fructose-1,6-diphosphate and are converted again to glucose-6-phosphate, via fructose-6-phosphate. This cycle is generally known as the "hexose-monophosphate shunt" (fig. 10).

Figure 10 shows that in one cycle a half molecule of glucose is catabolized. A

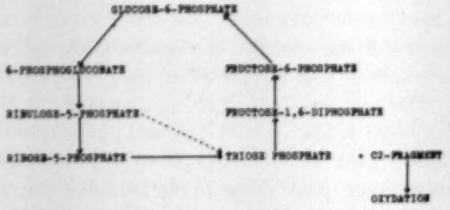


Fig. 10 (Müller, et al.). The hexose monophosphate shunt. (Horecker, 1951, slightly modified.)

rough indication of the extent of oxidative catabolism of the glucose by means of the "hexose-monophosphate shunt" is given by the oxidation of the glucose, which continues to occur after the addition of sodium fluoride (NaF). The "hexosemonophosphate shunt" traverses the NaF barrier. Dische, Munoz, Ehrlich, and von Sallmann (1953) consider it possible that this respiratory cycle, or a cycle similar in principle, is of great importance in the lens capsule.

In this manner the C_5 sugar can also be oxidized. Dische (1949) was, however, able to indicate another way in which this is possible, by the use of hemolized red blood corpuscles. According to this method, the ribose-5-phosphate can, without passing through this cycle, be synthesized to glucose-6-phosphate and then be catabolized in the usual manner. His findings were confirmed by Horecker (1951) with liver preparations.

b. *Dismutations associated with oxidative decarboxylations and carboxylations*

By far the largest part of the energy obtained by the catabolism of nutrients is formed oxidatively within the citric-acid cycle. A part of this energy is obtained by the oxidative decarboxylation of pyruvic acid and α-keto-glutaric acid. The dehydrogenating decarboxylation of the iso-citric acid is said, according to new investigations carried out by Salles and Ochoa (1950), also to be a uniform system. These steps of the citric-acid cycle can also take place in an anaerobic medium. In place of the respiratory chain system a different hydrogen acceptor must be added. This acceptor may, in

the cell, be a reaction whereby hydrogen is added, taking place in association with the oxidative decarboxylation. Such dismutations all take place, according to Hunter (1942a and b) with the absorption of phosphate. This fact should be of great importance in the case of the lens, the metabolism of which is largely anaerobic in character.

One of the most important forms of decarboxylation, which transforms malic acid to pyruvic acid with the help of the malic enzyme, was demonstrated by Heyningen and Pirie (1953) to be a reaction which was associated with the reduction of the glutathione in the lens. The occurrence of the malic enzyme was more marked in the lenticular nucleus than in the cortex. The TPN, the coenzyme of the malic enzyme, is continually oxidized by the glutathionreductase. It is still not clear in what way the glutathione is again oxidized in such a manner that this reaction can continue further.

Ames and Elvehjem (1947) discovered a glutathionoxydase which is a copper proteid and is therefore subject to inhibition by cyanide. Nothing is, as yet, known of the presence of this enzyme in the lens. Dische, Ehrlich, Munoz and von Sallmann did, nevertheless, find that the lens capsule is capable of oxidizing glutathione very rapidly. It may be that this discovery is important in connection with the problem of determining whether the course of a respiratory chain cycle, of the type of the hexose-monophosphate shunt, is accelerated or maintained by oxidization of the glutathione, which can serve as H_2-acceptor of the "Zwischenferment."

The reduction of glutathione in an anaerobic medium can be coupled, not only with the reaction of the malic enzyme, but also with the dehydrogenating decarboxylation of the isocitric acid to α-keto-glutaric acid, and also with the reaction of Warburg's "Zwischenferment," the dehydrogenation of the glucose-6-phosphate to phosphogluconic acid.

It would be interesting to investigate whether the lens is capable of allowing other dismutations to take place, such as occur in the remainder of the organism and are intimately associated with phosphate metabolism. For example, the following dismutation reactions have been proved in respect to the oxidative decarboxylation of α-keto-glutaric acid:

1) α-keto-glutaric acid + oxalacetic acid + H_3PO_4 + ADP = succinic acid + CO_2 + malic acid + *ATP*
2) α-keto-glutaric acid + acetoacetic acid + H_3PO_4 + ADP = succinic acid + CO_2 + β-oxybutyric acid + *ATP*

In a further dismutation part of the energy is used directly, to carry out the following synthesis:

α-keto-glutaric acid + α-keto-glutaric acid + NH_3 + H_3PO_4 + ADP = succinic acid + CO_2 + glutamic acid + *ATP*

The oxidative decarboxylations in an anaerobic medium are, partly, reversible. They are then coupled with energy-providing reactions such as that of the intermediate ferment. The following scheme gives an idea of the dismutation reactions in which the transference of hydrogen takes place by means of the codehydrase II:

Glutathione-S-S + TPN-H_2 = Glutathione-SH + TPN

↗ malic acid = pyruvate ; ↑ iso-citric acid = α-keto-glutaric acid ; ↖ glucose-6-phosphate = phosphogluconic acid

Glucose-6-phosphate + TPN = phosphogluconate + TPN-H_2

↙ pyruvate = malic acid ; ↓ α-keto-glutaric acid = iso-citric acid ; ↘ Glutathione-S-S = Glutathione-SH

There is a further respiratory by-path which avoids the cytochrome system. The hydrogen is directly transferred thereby from the flavin enzymes to the oxygen. The peroxide so formed is split up by peroxydase. In the catalytic reaction, which scarcely occurs in the cell, the whole of the energy is transformed into heat. In the peroxydase reaction the oxygen released is immediately used to bring about oxidization of a substratum. Phosphate metabolism has not been found to enter into this process.

5. Storage in phosphate compounds of the energy obtained

As was emphasized in the introduction, the central position of the phosphate metabolism consists in trapping the energy obtained by catabolism of nutrients and making this available again to the cell, in a form in which it can readily be used. This trapping occurs almost exclusively by means of the formation of ATP. In order to be able to cope with suddenly arising and heavy requirements of energy, the cell is able to create a store of energy for itself. For this purpose the cell transfers the phosphate of the ATP, at the same level of energy, to creatine. Both of the nonspecific phosphatases, that is, the alkaline and the acid, which are concerned in this reaction, have, on several occasions, been demonstrated to be present in the lens.

The creatine-transphosphorylase or creatine-kinase thus regenerates the ATP to ADP, so that this substance is constantly available as an energy-trapping reaction product. When the stored energy is mobilized, this process takes place in the reversed direction. Energy is generally made available only by ATP to processes requiring it. Nevertheless, according to Lang (1952), there are also endergonic processes, in which the energy released by the splitting up of creatine phosphate can be put to use without going through the bypath via ATP. An example of this, which he quotes, is the acetylation of choline to form acetylcholine.

It was possible to determine the creatine phosphate in the lens. Thus Rizzo (1937b) found from 2.4 to 3.3 mg. percent, on a fresh weight basis. Weekers and Süllmann (1938) state that it makes up some 5.0 to 10 percent of the mineral phosphate or from 1.0 to 2.0 percent of the acid-soluble phosphate. According to recent investigations of Nordmann and Mandel (1952 a and b) the young bovine lens contains 26.86, the young rabbit lens 18.09, and the young rat lens 18.5 mg. percent of phosphagene, again on a fresh weight basis. (These values were converted from the given phosphorus values to creatine phosphate.) Frohman and Kinsey (1952) determined the phosphagene content of various sections of the lens. The importance of the values determined by them will be dealt with in the following chapter on the localization of metabolism.

Even though an exact demonstration of the presence in the lens of the enzyme creatinekinase has not yet been made, this enzyme being needed for the transference of the phosphate group from ATP to creatine and, in the reverse direction, from phosphagene to ADP, it can nevertheless be assumed that the phosphagene in the lens has the same function as it has in the remainder of the organism.

There are still other forms of storage for energy phosphate, but these do not seem to play any part worth mentioning in the human organism. It is not to be supposed that, in this respect, the lens behaves differently from the remainder of the body, since these phosphate compounds and the enzymes necessary for their formation were not found in the lens. These are arginine phosphate, which assumes, in invertebrates, the function of the creatine phosphate, and acetyl phosphate, to which I have already referred.

If the requirements of the cell exceed the phosphate reserve, the cell can, with the help of myokinase or of ADP-phosphomutase, regenerate ATP molecules. Two ADP molecules thus form one molecule of adenylic acid and one molecule of ATP. It

would seem that this process has not been investigated, as yet, in the case of the lens.

Another possible means of energy transference, which is entirely different in principle, and is also possible without ATP, is that of transphosphorylation between two organic phosphate compounds. It is principally nucleotides and nucleic acids which come into consideration here. Phosphoric acid is said to be capable of transference, for example, to glycerine, from nucleotides via the alkaline phosphatase. In addition to this, the energy-rich phosphate combination of the nucleotides can be utilized in glycolysis, via the by-path which passes through ribose-1-phosphate (Kalkar, 1945, Schlenk and Waldvogel, 1947. The ribose-1-phosphate is rearranged to form ribose-5-phosphate and is split up into triose-phosphate and diose.

Localization of phosphate metabolism within the lens

Since the process of phosphate metabolism is most intimately connected with general metabolism, but most especially with oxidative metabolism, it is to be expected that the localization of the oxidative metabolism process should coincide with that of the most active phosphate metabolism. The fact that oxidative metabolism is not distributed uniformly over the lens is explained by the anatomic structure of this organ. The Warburg-Keilin system is not a soluble complex of enzymes, but is strictly connected with the mitochondria. We shall thus find the most active phosphate metabolism where mitochondria occur. This hypothesis has been experimentally confirmed. The work carried out by Frohman and Kinsey (1951, 1952) and by Nordmann and Mandel (1952a), has given a good deal of information concerning metabolic activity of the individual strata of the lens.

The former found that the cytochrome-cytochrome-oxydase system can probably only be demonstrated in the region of the lens epithelium. From this the authors conclude that only the lens epithelium possesses oxidative metabolism. This view is supported by the results which they give on the quantitative distribution of high energy phosphate. They were able to show that the ATP content of the capsule epithelium was the highest, that the figure was lower for the anterior cortex, that the content was still lower in the nucleus, and that it rose again in the posterior cortex and in the rear capsule. The same is true of pyruvic acid. These ratios were reversed for phosphagene and for lactic acid. Frohman and Kinsey draw the following conclusions from their results:

The epithelium has a metabolic process which is predominantly oxidative and thus receives the greatest amount of energy. In the other sections, where the respiratory ferments do not occur, the hydrogen obtained by catabolism of glucose cannot be transferred to the cytochrome system. Instead of this, it is transferred to the pyruvic acid, lactic acid being formed at the same time. Consequently, in these strata, there occurs an anaerobic catabolism of glucose. Since the energy gained from glycolytic catabolism is not adequate to maintain metabolism, the authors assume that the high-energy phosphate, which is formed in sufficient quantities in the epithelium, is continuously diffused from the epithelium to the inner strata of the lens, and is there used or stored as phosphagene. This hypothesis is very largely confirmed by their experimental results.

The results of Nordmann and Mandel (1952a) also agree with these findings. These authors investigated the quantitative distribution of the various phosphate esters of carbohydrate catabolism in the nucleus and in the cortex. They also found that both the ATP content and the content of the other phosphate esters are considerably higher in the cortex than in the nucleus. Palm (1948) and Dische (1951) had also come to the same conclusions. (See, in this connection, the section below on the occurrence of phosphates in the lens.)

If we may take the oxygen consumption

of a respiratory tissue as a measure of the gain in energy in the form of ATP, then, according to the investigations of Pignalosa (1939b) and Ely (1949), the metabolism of the lens capsule is not energy-forming, or is so only to a very limited extent. According to recent work by Dische and collaborators (1953) it is, neverthless, probable that the lens capsule also possesses its own metabolism. This may very well follow the course already described, partly via the hexosemonophosphate shunt. The experiments of the authors quoted demonstrate that the capsule is capable, when isolated, of oxidizing glutathione.

The fact that the process of phosphate metabolism takes places, for the most part, in the epithelium and in the external cortical strata, is also evident from the studies dealing with enzymes which act directly on the phosphate metabolism. Thus François and Rabaey (1951) were able to show that the phosphatases are localized in the equatorial region. They also occur in the lens capsule. Pyrophosphatase and adenosinetriphosphatase occur principally in the epithelium (Daily and collaborators (1951), Berardinis and Rosa (1952). In addition, Berardinis (1952) found that dehydrogenations only occur in the superficial fibrous strata of the lens and not in the nucleus.

We may thus summarize by saying that, on the basis of the results given by the authors named above, the lens epithelium has the most active phosphate metabolism, as would be expected from its very active general oxidative metabolism. The cortical strata are also capable of synthesizing ATP, wheras hardly any ATP can be shown to occur in the nucleus.

On the occurrence of phosphates in the lens

Total phosphate

Determinations of the total phosphate content of the lens have been made by several investigators. No important conclusions can be drawn from the values so obtained, as Nordmann (1954) in particular has pointed out. In some cases dry incineration and in other cases moist incineration was first applied and the phosphate content then determined by various methods. Even if reliably accurate methods of determination existed, we should still be unable to draw any conclusions concerning metabolic processes on the basis of these figures.

It is only the determination of the individual phosphate fractions which allows of any detailed study of phosphate metabolism. We would simply like to refer to the investigations of Fischer (1933), who found a lower total phosphate content in adult bovine lenses than in juvenile bovine lenses. On the other hand, Goldschmidt (1924) thinks that the total phosphate content of the human lens increases as the lens ages.

According to the investigations of Evans and Kern (1931) the ash of the normal canine lens contains from 1.7 to 4.7 percent of phosphorus, whereas the ash of the canine lens when affected by tetany cataract only contains an average of 1.1 percent of phosphorus. Mackay and collaborators (1932) determined (as an average value for four cases) a phosphate content of the normal human lens of 18.6 percent; this dropped to 8.3 percent in the case of cataracta senilis immatura, only to rise again to 11.1 percent in cataracta senilis matura. Salit (1943) found that, with progressive sclerosis, the total phosphate content in the ash of the normal human lens dropped from 10.34 percent to 4.17 percent. Salit and collaborators (1942) determined, in rats with galactose-cataract, a reduction in the phosphate content from 38.57 to 18.54 percent, on the basis of the ash weight of the lens. Thus we see that the content of phosphate in the ash of the lens decreases in senile cataract, tetany cataract, and galactose cataract.

Lüderitz (1937) incinerated histologic sections of the lens and made the phosphate content visible, using the method of Herrmann (1932). There exists a considerable difference between juvenile and adult hu-

man lenses. In the juvenile lens the coloration is distributed over the whole section, whereas in the adult lens it was frequently impossible to determine any phosphate at all. The most intensive coloration was found in the equatorial region. The nucleus used to accept the coloring substance less readily than the cortex; we may, perhaps, be allowed to conclude from this that the phosphate content of the various parts of the lens becomes smaller, the older the individual. In contrast to the epithelium, the capsule showed no presence of phosphate, when treated by this method.

Three main groups may be recognized within the total phosphate content:

a. Phospholipids
b. Protein phosphates
c. Acid-soluble phosphates

a. *Phospholipids*

The phospholipoids occur in the lens tissue, as also in every cell in the organism. The share of this phosphate compound in the total phosphate in the lens is probably 15 to 25 percent According to Krause (1935) the phospholipids represent some 60 percent of the total lipid content of the lens. They consist of lecithins, cephalins, and sphyngomyelines. The lecithins alone make up 65 percent of the phospholipids. According to D'Asaro, Young, and Williams (1954), the choline-containing phospholipids (lecithin and syphyngomyeline) make up over 50 percent of all the phospholipids. The total content of phosphatides of the bovine lens is given, by these authors, as 0.65 percent on a dry-weight basis.

Whether the other two fractions of the phospholipids, namely acetyl-phosphatide and the phosphatic acids, occur in the lens, does not seem to have been investigated, as yet, as a separate study. Relatively little is known of the importance of the phosphatides in the general cell metabolism. It is known that they are necessary for the maintenance of life. The interface activity of these compounds depends on their physicochemical properties. By reason of their polar structure they are capable of forming membranes. The compactness of these membranes depends on the concentration of the phospholipoids. Consequently, they are of importance with regard to the permeability to ions of the cell walls. Krause (1935) has pointed out that the phospholipids can take an active part in ion transport within the lens, since they are ampholytes, and are capable of binding ions.

No detailed knowledge is yet available, in connection with lens metabolism, concerning the frequently assumed function of the phospholipoids to transport fatty acids. One important task of the phospholipids of the lens is, according to Sauermann (1933), that the lecithins are capable of shifting the isoelectric point of the lens protein into the range of the lower pH values. This protects beta crystallines from precipitation, to which they are particularly susceptible.

The phospholipids, being amphoteric substances, are concerned in the maintenance of the constant level of hydrogen-ion concentration, precisely as the protein bodies. The phospholipids are probably of little importance as nutrients for the lens (Krause, 1935). By reason of the ease with which the phosphatide-protein bodies can be split up, they may affect the osmotic pressure of the lens; nevertheless, this effect may well be slight.

It is not yet known whether the phospholipids can be formed in the lens. We know that, in the case of the other cells, their formation is dependent on oxidative metabolism. This indicates that relatively large quantities of energy are necessary for their formation. Until now the presence of the enzymes necessary for this purpose has not been proved. According to Krause (1935) the phospholipids mostly occur in the lens in combination with cholesterol. Salit (1935) attributes the capacity of splitting up the phospholipids to the lens affected by cataract. The inorganic phosphate which is re-

leased in this process is said to be deposited as calcium phosphate.

Until some 20 years ago the findings concerning changes in the phospholipid content of the lens during aging and in the formation of cataract were contradictory. According to Salit, this contradiction depended on the fact that some of the investigators made use of cataractic lenses extracted outside the capsule, and that, in addition, the age of the subjects was left out of account. Salit concluded from these extensive investigations that, in the healthy human lens, a slight augmentation of the phospholipids occurs with increasing age. On the other hand, he found a clear augmentation of the phospholipids in the case of lenses affected by cataract with increasing age of the patients. Thus the phospholipid content of the lens affected by cataract rose from 0.453 mg. percent in the fifth decade of life to 0.533 mg. percent of fresh weight in the ninth decade of life. In addition to this Salit determined an average value of 0.534 mg. percent of fresh weight for incipient cataract and of 0.470 mg. percent for mature cataract.

b. *Protein phosphates*

This second main group of phosphate compounds in the cell, under which we would wish to class phosphoproteids and nucleic acids, has been little investigated, as yet, in the lens. A phosphoprotein with a phosphorus content of from 7.4 to 9.8 mg. percent was found by Mandel, Nordmann, Zimmer, and Harth (1949) in bovine and ovine lenses. In the trypsin digestion of the bovine lens they found that a small fraction of the phosphorus, which originated from this phosphoproteid, had been split off from ribonucleic acids. Exact investigations of the nucleic acids, which are so important for mitosis, seem to have been made, in the lens, only by Mandel, Nordmann, and Zimmer (1949); these authors found 42 to 47 mg. percent in the bovine lens and 33 to 36 mg. percent in the ovine lens of ribonucleic acid, on a fresh weight basis.

c. *Acid-soluble phosphates*

Among the acid-soluble phosphates we group together the phosphates which are dissolved in the acid cell extract after the protein has been precipitated. They comprise inorganic phosphate (orthophosphate), the intermediate phosphate esters, the nucleotides, for example, adenyl phosphates and phosphocreatine (phosphagen). They all take part in the catabolism of carbohydrates.

1. *Total acid-soluble phosphate*

Table 1 gives particulars regarding the content of acid-soluble phosphate in the crystalline lens of various types of animal. The investigations of H. K. Müller (1936, 1937c), Süllman (1937a), Brückner (1940), Nordmann and Mandel (1952b) and H. K.

TABLE 1

TOTAL ACID-SOLUBLE PHOSPHATE OF LENSES OF DIFFERENT ANIMALS IN MG. PERCENT FRESH WEIGHT
(Cited from the literature.)

	Müller 1936	Süllmann 1937	Müller 1937	Rizzo 1937	Müller 1939	Pignalosa 1937	Brückner 1940	Palm 1948	Milano 1941	Nordmann and Mandel 1952	Müller and Collaborators 1954
Calf	41.9	49.4	41.7	40.6			40.7			54.7	
Ox	36.3	31.5	34.7				32.3			33.8	
Rabbit, young			42.6		62.8	58.47	44.15	51.8		47.5	46.7
Rabbit, old										37.9	26.5
Horse							30.45				
Horse							21.76				
Dog							34.06				
Pig							35.08				
Cat, young							77.5				
Cat, old							35.5				
Rat, young										66.80	
Rat, old										60.25	
Human Lens									89.3		

Müller and collaborators (1954) show that the content of acid-soluble phosphate in the lens decreases as the subject gets older. Süllmann (1937a) attributed this decrease with age to a diminution in the capacity to form phosphate esters, and he does not believe that the lower permeability of the capsule of the lens of an older subject is responsible.

In cases of mature cataract the acid-soluble phosphate fraction may increase sharply, whilst the organic fraction disappears almost entirely. H. K. Müller (1936) found up to 200 mg. percent of inorganic phosphate, calculated on the fresh weight, in cattle cataract whilst the organic acid-soluble fraction had completely disappeared. In these cases there can be no doubt that an infiltration of phosphate must have taken place, and this is probably connected with the calcification of the cataractous lens. Similar findings were made by Updegraff (1932).

2. *Inorganic phosphate*

The opinion is very frequently put forward that a proportion of the inorganic phosphate is not present in the cell in the form of free ions but in an adsorptive combination.

The inorganic phosphate is determined in the acid lens extract by direct analysis. Palm (1948) and Nordmann (1954) rightly pointed out that the inorganic phosphate in the lens must be determined immediately after the death of the test animal. If this precaution is not observed, there may well be an increase in the inorganic phosphate content of the lens as a result of the action of phosphatase (particularly on the unstable phosphagen). In most investigations, particularly those where animals from slaughterhouses were used, an error must have crept in for this reason. Nordmann and Mandel (1952b) and Frohman and Kinsey (1952) are indeed the only workers who have determined the inorganic phosphate content while taking special precautionary measures. The former found a figure of 7.16 mg. percent on the fresh weight in the case of calf lenses. We ourselves have examined calf lenses two hours after death without employing any precautionary measures and apparently for this reason we obtained a mean figure of 7.6 mg. percent.

Table 2 summarizes a few of the findings of Nordmann (1954) in regard to the inorganic phosphate content of the lenses of various types of mammals. It may well be assumed that the figures for the individual species of mammal are of a similar order of size. The same applies to the lenses of various species of fish, as has been demonstrated by Brückner (1940).

The age of the animals has a marked influence on the inorganic phosphate content of the lenses. In this way, H. K. Müller and ourselves (1936b, 1939, 1954) as well as Nordmann and Mandel (1952b) have

TABLE 2

INORGANIC PHOSPHATE OF LENSES OF DIFFERENT ANIMALS IN MG. PERCENT FRESH WEIGHT
(Cited from the literature.)

	Süllmann 1937	Müller 1936	Rizzo 1937	Müller 1939	Pignalosa 1939	Brückner 1940	Palm 1948	Milano 1941	Nordmann and Mandel 1953	Müller and Kleifeld 1953b	Müller and Collaborators 1954
Calf	9.52		6.4			5.8			7.16	7.6	
Ox, young		9.6				7.2			6.20		
Ox, old		8.8									
Rabbit, young				13.4	20.87	8.85	8.6		5.30		8.70
Rabbit, old				12.6		6.15			4.30		6.50
Horse						7.63					
Dog						6.44					
Pig						6.1					6.81
Cat, young						5.78					
Cat, old						7.25					
Rat, young									4.56		
Rat, old									3.65		
Human Lens								46.7			

found in cattle, rabbits, and rats that there is a decrease in inorganic phosphate with advancing age. Brückner (1940), however, was only able to confirm this in the case of rabbits, whereas he found the opposite result in the case of cattle and cats. Nevertheless, these figures cannot be looked upon as decisive on account of the small numbers of tests carried out.

3. *Acid-soluble organic phosphate*

By acid-soluble organic phosphate we mean the difference between the total acid-soluble phosphate and the inorganic phosphate. This acid-soluble organic phosphate is built up of a large number of phosphoric acid esters. By following the procedure adopted by Lohmann (1928) we can divide these into fractions which are difficult to hydrolyze and fractions which are easy to hydrolyze. Of the easily hydrolyzed fractions, the fraction which is hydrolyzable in seven minutes plays a special part. This fraction contains the following phosphate compounds to a greater or lesser degree: ATP, glucose-1-phosphate, hexose diphosphate, phosphoenol-pyruvic acid and fructose-6-phosphate. The bulk of this fraction is made up of ATP and glucose-1-phosphate. The figures found for seven-minute hydrolyzable phosphate are shown in Table 3. It will be noted that as age advances there is a decrease in the amount of this phosphate fraction present in the lens.

If we subtract the amount of seven-minute hydrolyzable phosphate from the acid-soluble organic phosphate, we get what is known as the "residual phosphate." Phosphoglyceric acid, glycero-phosphoric acid, glucose-6-phosphate, and adenylic acid belong to this fraction. These figures for this fraction have only been determined on rare occasions. H. K. Müller (1936b) determined the content of this fraction in the lenses of young and old cattle. He found the quantity to decrease with age. The lenses of young cattle contained 24.8 mg. percent residual phosphate calculated on the fresh weight, while those of old cattle contained 18.2 mg. percent. Palm (1948) found 27.9 mg. percent residual phosphate calculated on the fresh weight in the case of rabbits. H. K. Müller and Kleifeld (1953a) found 18.6 mg. percent in young rabbits and 10.5 mg. percent in old rabbits, these figures being the mean for eight animals.

When determining the seven-minute hydrolyzable phosphate and the residual phosphate, what we are really doing is determining phosphate fractions each of which is made up of various phosphoric esters and where proportions of certain phosphoric esters occur in both fractions. This fact must be borne in mind when forming conclusions from the results.

As regards the individual acid-soluble phosphates, Rizzo (1937) and Weekers and Süllmann (1938) first undertook the determination of the phosphagen content. They found 2.4 to 3.3 mg. percent on the fresh

TABLE 3

SEVEN-MINUTE HYDROLYZABLE PHOSPHATE OF LENSES OF DIFFERENT ANIMALS IN MG. PERCENT FRESH WEIGHT

(Cited from the literature.)

	Palm 1948	Müller 1936	Müller and Kleifeld 1953	Kleifeld and Collaborators 1953	Müller and Collaborators 1954
Rabbit, young	15.3		12.1		15.4
Rabbit, old			8.0		9.1
Calf		7.5	7.7		
Ox		7.7			
Pig				10.05	9.08

TABLE 4

ESTER PHOSPHATE IN DIFFERENT PARTS OF A LENS OF A RABBIT IN MG. PERCENT FRESH WEIGHT
(Cited by Frohman and Kinsey, 1952.)

Fraction	Epithelium and Anterior Capsule	Anterior Cortex and Epithelium and Capsule	Anterior Cortex	Nucleus	Posterior Cortex	Posterior Capsule
Adenosine phosphates	14.26	1.86	1.55	<0.0062	0.62	3.41
Phosphocreatine	<0.775	0.62	0.31	<0.0155	2.48	1.86
Glucose-6-phosph.		18.6	19.84	2.79	6.82	
Hexosediphosphate		2.79	0.62	0.465	1.55	
Fructose-6-phosph.		4.03	1.24	0.62	1.24	
Inorganic phosphate		5.27	8.36	11.79	14.58	

weight (Rizzo) or 5.0 to 10 percent of the mineral phosphorus or 1.0 to 2.0 percent of the acid-soluble phosphorus (Weekers and Süllmann).

As recently as 1952 Frohmann and Kinsey and also Nordmann and Mandel determined for the first time the content of other acid-soluble phosphate esters in the lens. Their results are reproduced in Tables 4 and 5.

DISTRIBUTION OF ACID-SOLUBLE PHOSPHATE IN THE VARIOUS PARTS OF THE LENS

According to Palm (1948) the content of orthophosphate is more or less the same in the anterior and posterior capsules and in the equator in the case of cattle lenses. According to him, the highest concentration of seven-minute hydrolyzable phosphate and residual phosphate occurs in the equatorial region of the lens. However, the anterior capsule contains more of both fractions than the posterior capsule, and the latter in turn contains more than the nuclear region. Palm (1948) also found that the nucleus of the lens in cattle only contains one twenty-fifth of the seven-minute hydrolyzable phosphate present in the equator. Dische (1951), too, confirms Palm's observation that the anterior capsule of the lens contains more seven-minute hydrolyzable phosphate than the posterior capsule. These findings are all in agreement with the results of Lüderitz (1937) obtained in the section incinerations already mentioned.

The detailed determinations carried out by Frohman and Kinsey (1952), who investigated six different parts of the lens of rabbits in respect of their content of ATP + ADP, phosphagen, glucose-6-phosphate,

TABLE 5

ESTER PHOSPHATE AND INORGANIC PHOSPHATE OF LENSES OF DIFFERENT, YOUNG AND OLD MAMMALS IN MG. PERCENT OF FRESH WEIGHT
(Cited from Nordmann and Mandel, 1952.)

	Ox			Rabbit			Rat		Ox		
	Young	Old	Δ %	Young	Old	Δ %	Young	Old	Cortex	Nucleus	Δ %
Number of lenses	36	12		28	28		116	126			
Average weight of lenses (g)	1.059	2.531		0.304	0.578		0.039	0.055			
Adenosin phosph.	10.60	6.74	−36.4	13.00	8.21	−36.8	15.40	10.65	8.36	0.60	−93.0
Phosphocreatine	3.95	2.03	−48.6	2.66	1.37	−48.5	2.72	0.87	6.07	1.81	−70.2
Nucleotides of ATP	7.12	4.52	−36.5	7.58	4.74	−37.4	7.47	6.12	5.18	0.40	−92.5
Hexosediphosphate	1.12	0.91	−18.7	1.32	0.59	−55.4	1.17	1.28	—	—	—
Glucose-6-phosph.	4.79	4.00	−16.5	5.61	—	—	6.88	—	5.23	1.15	−78.0
Phosphoglyceric acid	4.45	2.39	−46.3	3.10	1.99	−35.9	2.22	2.19	0.55	0.20	−63.7
Free adenylic acid	2.72	2.33	−14.2	3.58	2.87	−19.9	2.78	1.84	1.81	0.60	−66.9
Glucose-1-phosph.	1.81	0.93	−48.6	2.41	1.28	−46.9	1.63	2.00	1.10	0.21	−81.0
Glycerophosphate	8.82	5.93	−32.8	11.70	8.57	−26.8	6.45	3.79	7.40	2.83	−61.7
Propandiolphosph.	4.19	3.14	−25.1	—	—	—	3.44	—	2.47	0.24	−90.3
Phosphorus total	54.7	33.8	−38.2	47.50	37.90	−20.2	66.80	60.25	60.68	19.50	−67.8
Inorganic phosph.	7.16	6.20	−13.4	5.30	4.30	−18.9	4.56	3.65	8.54	6.38	−25.2

hexose diphosphate, and fructose-6-phosphate provide a very thorough survey of the location of these phosphate compounds in the lens (table 4). Similar researches, but involving the investigation of a larger number of compounds, were carried out by Nordmann and Mandel (1952b), and in these they also reported on the differences due to age in the lenses of cattle, rabbits, and rats (table 5).

On the absorption of phosphate in the lens

The penetration of phosphate from the aqueous humor or nutrient solution into the lens has been the subject of detailed study by Palm (1948, 1954), von Sallmann and collaborators (1951), H. K. Müller and Kleifeld (1952a, b, 1953a, b) and also by Christianssen and Palm (1954).

If a cattle lens is placed in a nutrient solution which contains inorganic radio-active P^{32}, then after a test lasting 41 minutes radioactive phosphate is found in the marginal zones of the lens, as has been demonstrated by Palm with the help of radio-autograms. The same was found by von Sallmann and Locke (1951) and also by Christianssen and Palm (1954) in experiments on rabbit lenses in vivo. When the experiment was carried out in this way there was no radioactive phosphate to be found in the lens nucleus. We can confirm this observation. After the lenses had been kept for two hours in a nutrient solution containing P^{32}, we dissected them into three parts as shown in Figure 11. When the axial cylinder was dissected perpendicular to its axis into sections approximately 150 to 600 microns thick, it was found that the P^{32} concentration was highest in the sections nearest to the poles of the lens. There was very little or no radioactive phosphate ascertainable in the parts of the cylinder corresponding to the nucleus of the lens (table 6).

There are two main possibilities as regards this penetration of inorganic phosphate from the aqueous humor into the lens. It may penetrate into the lens either by diffusion or by active transportation (passive and active absorption). According to the researches of Palm (1948) and Müller and Kleifeld (1953b), active metabolic processes play an important part in the entry of phosphate into the lens. In this way Palm (1948) has been able to demonstrate that within a few minutes of placing a rabbit lens in a nutrient solution which contained traces of labelled inorganic phosphate, the inorganic phosphate taken up was already

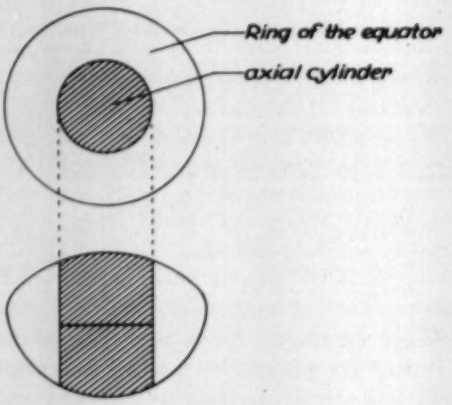


Fig. 11 (Müller, et al.). Division of the lens by a trephine. The different parts of the lens are shown in upper and side view.

TABLE 6

P^{32} distribution in the axial cylinder of a rabbit lens

(See fig. 11.) (Slice 1 upper layer of the anterior pole; Slice 9 about two mm. below the surface of the lens.)

Number of the Slice	Diameter of Height of the Slice [mm]	Counts/min. per 1 mg of the Slice	Amount in % of Total Counts
1	0.145	139.3	73.0
2	0.154	41.9	22.0
3	0.250	9.2	4.8
4	0.630	0.4	0.2
5	0.186	0	—
6	0.177	0	—
7	0.211	0	—
8	0.170	0	—
9	0.209	0	—
Total:	2.132	190.8	100.0

in organic combination. Among other things Palm (1948) also found that after the lens had been kept for 10 minutes in a nutrient solution containing phosphorus isotope, 40 percent of the inorganic P^{32} which had penetrated had already been incorporated into the seven-minute hydrolyzable phosphate fraction of the lens.

In the opinion of Hevesy (1940) any phosphorus brought into the organism in the inorganic form is not exchanged with the phosphorus found in the organic phosphate, unless catabolism and resynthesis have taken place. If Palm (1948) found the radioactive inorganic P^{32} occurring principally in organic combination, this is therefore proof that during the period of the experiment there took place a synthesis in which P^{32} was incorporated.

Palm (1948) obtained his results by measuring the activity of the individual fractions after separating them on the basis of different hydrolysis times. Müller and Kleifeld (1953a), following the method adopted by Schild and Maurer (1952), separated the labelled phosphoric esters by means of paper electrophoretic tests on the lens extract. In this way they obtained three differentiated groups of substances.

Figure 12 shows the position of the fractions determined. The evaluation of these was carried out by the radiometric method by measuring the impulses per minute per electrophoretic track. According to our own investigations, Maximum III is composed almost exclusively of ATP. Maximum I consists of the P^{32} incorporated in the inorganic phosphate. Maximum II is composed of P^{32} which is chiefly incorporated in the phosphate fractions which are only hydrolyzed with difficulty but also contains easily hydrolyzable portions. We refer to this as "residual phosphate" although we know that this is not exactly identical with the acid-soluble organic phosphate minus the seven-minute hydrolyzable phosphate.

In line with the results obtained by Palm (1948) on rabbit lenses, we also found

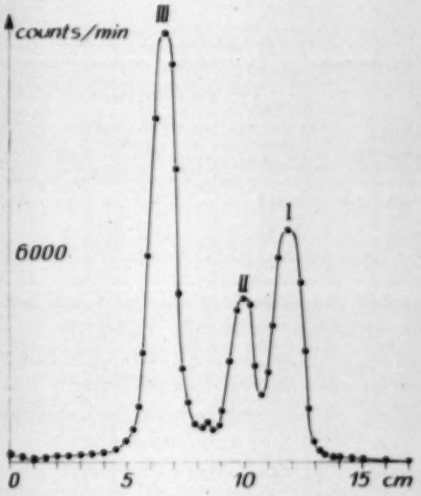


Fig. 12 (Müller, et al.). P^{32} distribution after separation by paper electrophoresis of an aqueous extract of the lens of a young rabbit.

(1952b, 1953a, b, 1954) with human lenses as well as cattle, calf, pig, and chicken lenses that the labelled inorganic phosphate is incorporated mainly in the seven-minute hydrolyzable fraction.

These investigations already made it appear probable that there is an active transportation of phosphate into the lens. Müller and Kleifeld (1953b) were able to prove this. They showed that the intake of phosphate into the lens can to a great extent be inhibited by KCN, iodine monoacetic acid, and NaF (table 7). In spite of this, however, it is of course possible that a part of the inorganic P^{32} penetrates into the lens by way of diffusion.

The inhibition brought about by the enzyme inhibitors does not depend on the diminution of the permeability of the capsule. In this way, tests carried out on the isolated anterior and posterior capsule of cattle lenses with and without KCN or JCH_2COOH did not show a decreased but an increased permeability to P^{32} when these enzyme inhibitors were added. In the case of sodium fluoride, too, the mean values showed an increase in the permeability of the cap-

TABLE 7

COUNTS/MIN. PER ONE GM. LENS IN PERCENT OF COUNTS/MIN. OF ONE CM.³ BATH SOLUTION AFTER FOUR HOURS' INCUBATION IN A BATH SOLUTION WITH AND WITHOUT ADDITION OF ENZYME INHIBITORS

Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	Average Weight of Lenses (in gm.)	Addition to Bath-Solution	P^{32}-Uptake in %
14	0.402	51.5±4.7	0.409	KCN	14.4±2.6
13	0.421	57.2±5.0	0.424	$CH_2|\cdot COONa$	22.0±3.15
10	0.382	63.6±5.2	0.406	NaF	24.3±3.0

sule, but the difference observed has not been confirmed statistically (table 8).

As the enzyme inhibitors mentioned bring about an inhibition of the carbohydrate metabolism, we may assume that the assimilation of P^{32} is dependent upon the energy supplied in the catabolism of carbohydrates. The correctness of this assumption is borne out by our observation that any inhibition of the assimilation occurs in conjunction with a decrease in the absolute content of seven-minute hydrolyzable phosphate (table 9).

In addition, the incorporation of inorganic P^{32} into the several organic phosphate fractions is affected in a characteristic manner by the enzyme inhibitors (table 10). In this way, KCN, iodine monoacetic acid, and NaF bring about a decrease in the amount incorporated into the ATP. Furthermore KCN inhibits incorporation into the "residual phosphate fraction." As a result of the addition of NaF the P^{32} content of this phosphate fraction is increased, and this is perhaps also the case when iodine monoacetic acid is added. These differences are based on the fact that the enzyme inhibitors are effective at different stages of the catabolism of carbohydrates. The effects of sodium fluoride and iodine monoacetic acid also differ in respect of the inorganic fraction.

In addition, in Figure 13 we have recorded all the results we have available regarding absorption and we have plotted these against the absolute content of seven-minute hydrolyzable phosphate, obtaining in this way a direct linear relationship (correlation coefficient $r = 0.722$ for 148 cases). As a great part of the seven-minute hydrolyzable fraction consists of high-energy ATP we believe that there is a close connection between the ATP content of the lens and its capacity to absorb phosphates.

According to the observations of Frohman and Kinsey (1952) and also those of Nordmann and Mandel (1952a) we must look

TABLE 8

TESTS ON ISOLATED ANTERIOR AND POSTERIOR CAPSULE* OF CATTLE LENSES

Number of Experiments	Average weight of Lenses (in gm.)	Kind of Used Capsule	Addition	Counts/min. of Test Solution in % of Counts/min. of Bath-Solution	Average Weight of Lenses (in gm.)	Kind of Used Capsule	Addition	Counts/min. of Test Solution in % of Counts/min. of Bath-Solution
9	2.094	A	—	12.5±2.22	2.088	A	KCN	32.3±3.03
5	2.234	P	—	22.6±2.73	2.220	P	KCN	40.2±3.24
4	1.196	A	KCN	17.3±1.27	1.991	P	KCN	14.7±2.29
10	2.239	A	—	12.0±1.19	2.250	A	$CH_2|COONa$	16.0±1.40
10	2.118	A	—	14.2±1.44	2.149	A	NaF	18.0±3.26

A = anterior capsule.
P = posterior capsule.

TABLE 9

ACID-SOLUBLE PHOSPHATES OF YOUNG AND OLD RABBIT LENSES INCUBATED IN BATH SOLUTION WITH AND WITHOUT ADDITION OF ENZYME INHIBITORS FOR FOUR HOURS

Number of Experiments	Average Weight of Lenses (in gm.)		Averages in mg % P			
			Inorganic Phosphate	7-min. Hydrolyzable Phosphate	"Residual-Phosphate"	Total Acid-Soluble Phosphate
8	0.287	young	9.1±0.66	12.1±0.39	18.6±1.08	39.8±2.11
8	0.535	old	6.3±0.22	8.0±0.19	10.5±1.15	24.7±1.04
4	0.355	KCN	13.8±0.79	3.5±0.43	16.5±0.83	33.8±1.5
4	0.307	$CH_3 \cdot COONa$	12.0±0.41	3.6±0.35	20.6±1.0	36.2±1.6
4	0.305	NaF	9.1±0.07	5.5±0.39	20.8±0.67	35.2±0.99

upon the epithelium of the lens as the important site for the elaboration of ATP. It may therefore be that there are different conditions for phosphate absorption at the front of the lens and at the back. For this reason Palm (1948) made separate investigations of the absorption of phosphate on the front and rear surfaces of the lens. He found that the amount of phosphate which penetrated through the posterior surface was slightly less than that which penetrated through the anterior surface. However, Palm does not feel justified in accepting this as proved, in view of the difference in curvature of the two surfaces of the lens.

In the course of experiments on rabbits in vivo Christiansson and Palm (1954) found radioactive phosphate which had penetrated into the region of the anterior surface of the lens one to four hours after the intraperitoneal injection of P^{32}. This must not be the result of differences in the absorptivity of the anterior and posterior surfaces of the lens, but is probably due to the fact that in vivo the injected P^{32} is offered more rapidly and in greater quantities to the anterior surface than to the posterior surface.

Palm (1948) also established by his tests in vitro that the incorporation into the residual phosphate (that is to say the acid-soluble organic phosphate less the seven-minute hydrolyzable phosphate) takes place to a greater extent on the anterior surface of the lens than on the posterior surface. He believes that this difference is linked up with the function of the epithelium of the lens in the oxidative catabolism of carbohydrates.

TABLE 10

P^{32} DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS WHICH WERE SEPARATED BY PAPER ELECTROPHORESIS AFTER FOUR HOURS' INCUBATION OF RABBIT LENSES IN A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT THE ADDITION OF ENZYME INHIBITORS

Number of Experiments	Average Weight of Lenses (in gm.)		P^{32}-Distribution in % Among		
			Inorganic Phosphate	ATP	"Residual-Phosphate"
6	0.405	—	20.3±4.7	51.2±1.9	28.5±4.8
6	0.413	KCN	55.5±8.9	26.7±3.8	17.8±5.8
			+35.2	−24.5	−10.7
5	0.395	—	29.1±1.6	51.9±1.8	19.0±0.3
5	0.366	$CH_3 \cdot COONa$	56.6±5.0	11.8±2.1	31.6±2.9
			+27.5	−40.1	+12.6
9	0.439	—	28.0±3.9	51.4±1.6	20.6±2.6
9	0.428	NaF	23.8±1.2	34.2±1.7	42.0±1.6
			− 4.2	−17.2	+21.4

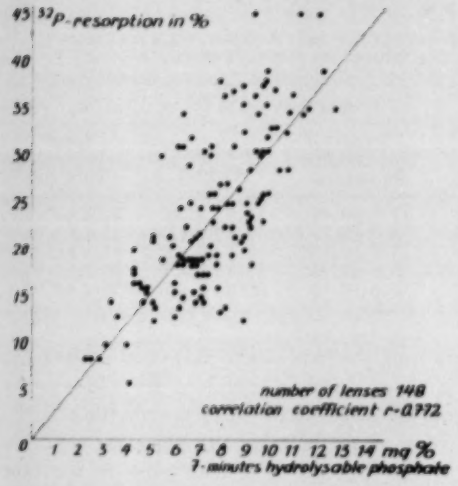


Fig. 13 (Müller, et al.). Dependence of P^{32} resorption of rabbit lenses on their contents of seven-minute hydrolyzable phosphate.

We have carried out a number of investigations similar to those of Palm and we have made separate examinations of the intake of phosphates by the anterior and posterior surfaces of twin lenses of rabbits and calves. As will be seen from Table 11, in the course of these experiments more phosphate passed into the lens through the anterior surface of the rabbit lens than through the posterior surface. I share Palm's view that the results of tests of this sort must be accepted with caution. In addition, we have to report that we could not find this distinction in the case of calf lenses. However, unlike Palm, we were not able to ascertain a difference in the incorporation of P^{32} into the organic phosphate fraction either with rabbit lenses or with calf lenses. The results of our electrophoretic investigations as set out in Table 11 show that incorporation into the "residual phosphate" took place to approximately the same extent (with the margin of error) whether the phosphate penetrated through the posterior surface or through the anterior surface, and this was the case both with rabbit and calf lenses. Further investigations are required to show whether the difference in the results of Palm's investigations and our own are due to the fact that the phosphate fractions which he and we lump together under the designation "residual phosphate" are not absolutely identical.

In the case of rabbit lenses it proved possible by the addition of potassium cyanide to inhibit the absorption both through the anterior surface and also through the posterior surface. As may be seen from Tables 12 and 13, the inhibitive effect was somewhat stronger where the phosphate penetrated through the anterior surface than where it was absorbed through the posterior surface. We found differences which were fundamentally the same in the case of calf lenses. Nevertheless, in the case of calf lenses the differences were too small in relation to the margin of error to permit us to make a definite pronouncement regarding them.

In all cases, with both rabbit and calf lenses, the addition of KCN brought about a distinct decrease in the amount of P^{32} incorporated into the ATP. The decrease in the amount of P^{32} incorporated into ATP was quite independent of the penetration of

TABLE 11

P^{32} UPTAKE IN PERCENT AND DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF RABBIT AND CALF LENSES. THE ANTERIOR AND POSTERIOR PARTS OF THE LENSES, RESPECTIVELY, HAD BEEN IN CONTACT WITH A BATH SOLUTION CONTAINING P^{32} FOR TWO HOURS

Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			
			Inorganic Phosphate	ATP	"Residual Phosphate"			Inorganic Phosphate	ATP	"Residual Phosphate"	
6	0.405	10.3 ± 2.02	38.2	39.8	22.0	0.407	6.0 ± 1.05	39.9	42.3	17.8	Rabbit
6	1.012	1.1	46.4	45.5	8.1	1.013	1.2	50.2	40.1	9.7	Calf
		anterior part of the lens incubated					*posterior part of the lens incubated*				

TABLE 12

P^{32} UPTAKE IN PERCENT AND DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF RABBIT AND CALF LENSES. THE POSTERIOR PART OF THE LENSES HAD BEEN IN CONTACT WITH A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT THE ADDITION OF KCN FOR TWO HOURS

Without KCN						With KCN					
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses in (gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			
			Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"	
8	0.297	2.8±0.11	28.4	49.2	22.4	0.297	1.9±0.13	54.1	25.9	20.0	Rabbi
4	0.970	1.6±0.1	33.9	54.7	11.4	0.970	1.1±0.3	65.9	23.7	10.4	Calf

P^{32} through the anterior or posterior surface of the lens.

A state of affairs which is fundamentally different is revealed, if the phosphate absorption is studied in the decapsulated lens.

If one of the two lenses of a rabbit is decapsulated and placed in a nutrient solution containing P^{32}, the decapsulated lens will take up more radioactive phosphate than the intact lens during the first 10 minutes, as shown in Table 14. If the lenses are kept in the nutrient solution for 20 minutes, the amount of phosphate taken up is approximately the same, and then if the lenses are left in for a still longer period, more phosphate is found in the intact lens than in the one which has been decapsulated. This result is bound up with the fact that when the decapsulated lens is kept for longer periods in the nutrient solution it loses its superficial layers of fibers. This loss may cause the wrong impression that there is a greater absorption of phosphate into the intact lens as compared with the decapsulated lens. Comparisons between the phosphate absorption of the intact lens and the decapsulated lens may therefore only be made if the lenses are kept in the solution for less than 20 minutes.

We must therefore conclude that during the first 10 minutes the decapsulated lens takes up more phosphate than does the intact lens. Active absorption plays an unimportant part—if any at all—in this taking up of phosphate into the decapsulated lens, because as may be seen from Table 15, the penetration of P^{32} into the decapsulated lens cannot be affected either by KCN or by iodine monoacetic acid. It is therefore probable that the inorganic phosphate penetrates by diffusion into the lens fibers deprived of capsule and epithelium.

From the figures shown in Table 16 it will be seen that even when they are deprived of capsule and epithelium the lens fibers are capable of incorporating the P^{32} into the organic fractions, and particularly into ATP. This incorporation into ATP is decreased by the addition of sodium fluoride and iodine monoacetic acid (tables 17 and 18). This inhibition of the incorporation of this phosphorus when NaF is added proceeds hand in hand with an increase of the amount incorporated into the "residual phosphate." It

TABLE 13

P^{32} UPTAKE AND DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF RABBIT AND CALF LENSES. THE ANTERIOR PART OF THE LENSES HAD BEEN IN CONTACT WITH A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT THE ADDITION OF KCN FOR TWO HOURS

Without KCN						With KCN					
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			
			Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"	
3	0.312	3.5±0.25	20.1	53.8	26.1	0.313	1.2±0.30	62.3	22.3	15.4	Rabbit
11	1.039	1.4±0.07	33.8	56.1	10.1	1.039	0.8±0.09	64.3	25.6	10.1	Calf

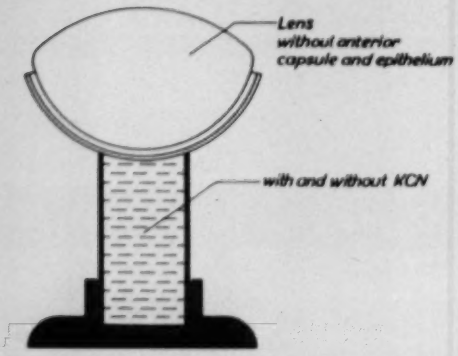


Fig. 14 (Müller, et al.). Diagram to show posterior surface of rabbit lens in contact with bath solution.

must, however, be emphasized that in the case of the decapsulated lens potassium cyanide causes no detectable disturbance of the incorporation of the P^{32} into the organic phosphate fractions (table 18).

To sum up, this means that when the capsule and the epithelium are removed, the capability of the lens in respect to the active absorption of phosphate decreases. We must therefore assume that the location of the processes which bring about the active absorption of phosphates is to be found in the capsule epithelium system. As these processes are capable of inhibition by KCN, NaF, and iodine monoacetic acid, it is probable that they are closely connected with the oxidative catabolism of the carbohydrates. Another fact in favor of this assumption is that the capability of absorbing phosphate is dependent upon the ATP content of the lens.

In the decapsulated lens, on the other hand, the absorption of phosphate cannot be influenced by KCN, NaF, or iodine monoacetic acid and the incorporation of the P^{32} into the organic phosphate fractions is not changed by KCN, but is affected by NaF and by iodine monoacetic acid. This would suggest that in the decapsulated lens the incorporation of the P^{32} into the organic phosphate fractions comes about by glycolysis. The mechanical removal of the capsule and epithelium causes no important qualitative change in the incorporation of the P^{32} into the various phosphate fractions. Damage to the capsule-epithelium system by potassium cyanide, however, causes a change in the process of this incorporation. This striking difference between the effect of the mechanical removal of the capsule and epithelium and the damaging of the capsule and epithelium by KCN must be based on processes which take place in the capsule and the layer of lens fibers which are in contact with it, but not in the epithelium.

In fact, if one removes the anterior capsule of the lens and the epithelium up to just above the equator, using the phase contrast microscope to keep a check on this process, and then places the lenses so that only the posterior surface is in contact with

TABLE 14

P^{32} UPTAKE IN PERCENT AFTER INCUBATION OF INTACT RABBIT LENSES AND RABBIT LENSES WITHOUT CAPSULES

Intact Lenses			Lenses Without Capsule		
Time of Incubation in Min.	Weight of Lens (in gm.)	P^{32}-Uptake in %	Weight of Lens (in gm.)	P^{32}-Uptake in %	Difference in % Between P^{32}-Uptake of the Lens Without Capsule and the Intact Lens
5	0.325	0.5	0.324	5.1	+1060.0
10	0.293	1.7	0.292	7.7	+ 351.0
20	0.276	6.2	0.277	5.3	− 14.5
40	0.286	11.4	0.287	5.5	− 51.2
80	0.272	28.3	0.274	5.2	− 81.6
120	0.280	48.5	0.280	4.1	− 91.4

TABLE 15

P^{32} UPTAKE IN PERCENT OF RABBIT LENSES WITHOUT CAPSULE AFTER INCUBATION IN A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT ADDITION OF ENZYME INHIBITORS

Time of Incubation in Min.	Weight of Lens (in gm.)	P^{32}-Uptake in %	Weight of Lens (in gm.)	Addition	P^{32}-Uptake in %
5	0.322	4.2	0.322	KCN	4.2
10	0.344	6.1	0.342	KCN	6.9
20	0.338	10.5	0.346	KCN	9.8
5	0.350	5.5	0.350	$CH_3]\cdot COONa$	5.7
15	0.338	9.4	0.336	$CH_3]\cdot COONa$	9.4

TABLE 16

P^{32} DISTRIBUTION IN PERCENT AMONG THE PHOSPHATE COMPOUNDS DURING INCUBATION IN A BATH SOLUTION CONTAINING P^{32} OF INTACT LENSES OF RABBITS AND LENSES WITHOUT CAPSULES

Intact Lenses					Lenses Without Capsule				
Time of Incubation	Average Weight of Lenses (in gm.)	P^{32}-Distribution in % Among			Time of Incubation	Average Weight of Lenses (in gm.)	P^{32}-Distribution in % Among		
		Inorganic Phosphate	ATP	"Residual Phosphate"			Inorganic Phosphate	ATP	"Residual Phosphate"
5′	0.325	18.6	54.4	27.0	5′	0.324	31.8	46.6	21.6
	0.395	29.2	53.6	17.2		0.394	26.6	63.6	9.8
10′	0.293	20.2	63.6	16.2	10′	0.292	26.9	55.3	17.8
	0.336	23.6	50.7	25.7		0.336	25.7	51.8	22.5
20′	0.276	11.8	57.9	30.3	20′	0.277	11.3	62.6	26.1
	0.309	16.2	58.6	25.2		0.311	23.1	43.0	33.9

TABLE 17

P^{32} DISTRIBUTION IN PERCENT AMONG THE PHOSPHATE COMPOUNDS DURING TWO HOURS' INCUBATION OF RABBIT LENSES WITHOUT CAPSULES IN A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT ADDITION OF ENZYME INHIBITORS

Number of Experiments	Average Weight of Lenses (in gm.)	Enzyme Inhibitor	P^{32}-Distribution in % Among					
			Inorganic Phosphate		ATP		"Residual Phosphate"	
7	0.254	—	41.0	±3.8	40.0	±2.9	19.0	±1.4
7	0.259	$CH_3]\cdot COONa$	73.0	±1.4	9.0	±0.53	18.0	±1.07
			+32.0		−31.0		−1.0	
4	0.218	—	49.2	±5.5	35.8	±2.4	15.0	±2.8
4	0.215	NaF	47.5	±4.9	19.8	±1.6	32.7	±3.9
			−1.7		−16.0		+17.7	

TABLE 18

P^{32} DISTRIBUTION IN PERCENT AMONG THE PHOSPHATE COMPOUNDS DURING INCUBATION OF THE LENSES OF RABBITS WITHOUT CAPSULES IN A BATH SOLUTION CONTAINING P^{32} WITH AND WITHOUT ADDITION OF KCN (1:1,000)

Intact Lenses					Lenses Without Capsule					
Time of Incubation	Average Weight of Lenses (in gm.)	P^{32}-Distribution in % Among			Time of Incubation	Addition to Bath Solution	Average Weight of Lenses (in gm.)	P^{32}-Distribution in % Among		
		Inorganic Phosphate	ATP	"Residual Phosphate"				Inorganic Phosphate	ATP	"Residual Phosphate"
5′	0.323	20.5	63.6	16.2	5′	KCN	0.322	18.5	67.9	13.6
10′	0.344	13.3	65.3	21.4	10′	KCN	0.342	16.8	58.8	24.4
20′	0.338	8.7	71.6	19.7	20′	KCN	0.360	33.7	59.3	7.0
40′	0.246	9.5	57.1	33.4	40′	KCN	0.246	25.6	54.2	20.2

the nutrient solution containing P^{32}, it is found (table 19) that there are only slight differences between the lenses with anterior capsule and those without when it comes to the absorption of phosphate and the incorporation of P^{32} into ATP. This would suggest that the absorption of phosphate through the posterior surface of the lens is to some extent independent of the function of the epithelium of the lens.

When KCN was, however, added to the nutrient solution for the lenses which had no anterior capsule and no epithelium, and when these lenses were placed in such a way that they were in contact with the nutrient solution only in the region of the posterior surface, it was found that there was a distinct inhibition of the incorporation of P^{32} into ATP, as will be seen from Table 20.

This distinction became even more apparent when the lens was dissected into three parts for analysis, that is, an equatorial ring and an anterior and posterior axial cylinder (fig. 11). The posterior axial cylinder, as will be seen from Table 21, showed a considerable decrease in the amount of P^{32} incorporated into ATP, and at the same time there was a decreased absorption of P^{32} into this part of the lens. We thus see that the entry of P^{32} into the lens fibers through the posterior capsule is not only more or less independent of the function of the epithelium, but it is also affected by KCN and its incorporation into ATP depends to some extent on processes which are sensitive to KCN.

As we have found that the isolated posterior capsule becomes more permeable to P^{32} as a result of the effect of KCN, and as the investigation of Dische and his collaborators (1953) have demonstrated that there is no metabolic process sensitive to KCN in the metabolism of the capsule, we must content ourselves for the time being with the assertion that in the interplay between the posterior capsule and the lens fibers there are metabolic processes which can be disturbed by KCN and on which the absorption of P^{32} and its incorporation into ATP depend.

TABLE 19

P^{32} UPTAKE IN PERCENT AND DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF RABBIT LENSES. BEFORE STARTING THE INCUBATION, THE ANTERIOR CAPSULE AND EPITHELIUM OF ONE OF THE LENSES WERE REMOVED. THE POSTERIOR PART OF THE LENSES HAD BEEN IN CONTACT WITH A BATH SOLUTION CONTAINING P^{32} FOR TWO HOURS

	Intact Lenses					Lenses Without Anterior Capsule and Epithelium				
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among		
			Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"
8	0.334	2.8±0.187	33.8	47.7	18.5	0.334	2.5±0.132	46.9	39.1	14.0

TABLE 20

P^{32} UPTAKE IN PERCENT AND DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF RABBIT LENSES WITHOUT ANTERIOR CAPSULE AND EPITHELIUM. THE POSTERIOR PART OF THE LENSES HAD BEEN IN CONTACT WITH THE BATH SOLUTION FOR TWO HOURS. THE SOLUTION FOR THE ONE LENS CONTAINED KCN

Without KCN						With KCN				
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among		
			Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"
8	0.344	2.4±0.107	48.4	35.2	16.4	0.346	2.9±0.25	61.4	19.8	18.8

Dependence of the phosphate metabolism of the lens on age

We know that as age increases the carbohydrate metabolism of the lens undergoes certain changes. In this way, the lens of an old animal takes up less sugar because the sugar content of the aqueous humor decreases with age (Müller, 1938), because the permeability of the capsule decreases (Friedenwald, 1930a), and because the capacity for active sugar absorption decreases with advancing age (Müller, 1937b).

From the investigations of O'Brien and Salit (1931), H. K. Müller (1943, 1936a) and Krause (1938) we also know that during the course of life the glucose content of the lens decreases. Furthermore, both Müller (1936a) and Vicentiis and Auricchio (1951) have shown that the sugar consumption of the lens decreases as the age of the subject increases.

A similar state of affairs has been demonstrated in respect to lactic acid. For instance, Weekers (1937, 1941) as well as Mandel and Zimmer (1952) found the lactic-acid content of the lenses of calves to be higher than that of the lenses of grown cattle. In addition, Leinfelder and Christiansen (1952) have demonstrated that the formation of lactic acid in the lens of a young rabbit is two to three times greater than in the lenses of older rabbits.

A decrease due to age in the amount of pyruvic acid in the lenses was observed by Fischer (1938) and also by Mandel and Zimmer (1952).

These changes in the carbohydrate metabolism which are bound up with the age of the subject naturally go hand in hand with changes in the phosphate metabolism.

Müller (1936b, 1937c), Süllmann (1937a), Brückner (1940), Nordmann and Mandel (1952), and we ourselves (1954) have found a decrease in the acid-soluble phosphate as the age of the subject increases. This is based on a decrease in all the components which form the acid-soluble phosphate in the lens. This means that there is a decrease in the inorganic phosphate (Müller 1936b, 1939); Brückner (1940), Nordmann and Mandel (1952); and ourselves (1954) in the seven-minute hydrolyzable phosphate (Müller and Kleifeld, 1953b) and in the residual phosphate (= acid-soluble or-

TABLE 21

P^{32} UPTAKE IN PERCENT AND DISTRIBUTION IN PERCENT AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF THE POSTERIOR PART OF THE AXIAL CYLINDER OF RABBIT LENSES. AFTER TAKING OFF THE ANTERIOR CAPSULE AND EPITHELIUM, THE LENSES HAD, ON THEIR POSTERIOR PART, BEEN IN CONTACT WITH A BATH SOLUTION CONTAINING P^{32} FOR TWO HOURS. THE SOLUTION FOR THE ONE LENS CONTAINED KCN

Without KCN						With KCN				
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among		
			Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"
8	0.071	7.1±1.28	40.5	42.4	17.1	0.070	4.1±0.7	74.2	10.9	13.3

ganic phosphate minus seven-minute hydrolyzable phosphate) (Müller, 1936b; Müller and Kleifeld, 1953b).

The dependence of the seven-minute hydrolyzable phosphate content upon the weight of the lens and consequently upon the age of the subject is an exponential function, as will be seen from Figure 15. Although this is a compilation of the results of tests which were carried out with other objects in view, and although therefore the seven-minute hydrolyzable phosphate content of the lenses was not determined until the lenses had been kept in a nutrient solution for two hours, this should only have a quantitative effect on the result and not a qualitative one.

Figure 16 shows that the relationship between the decrease in inorganic phosphate and the weight of the lens is a linear function. This difference in the relationship to the age of the subject on the part of the seven-minute hydrolyzable phosphate on the one hand and of the inorganic phosphate on the other is apparently due to the differences in the contents of these phosphates as between the cortex and the nucleus. In point of fact, the nucleus of the lens contains practically no seven-minute hydrolyzable phosphate, whereas the cortex contains a large amount. In contrast to this, the cortex of the lens contains only slightly more inorganic phosphate than the nucleus. We assume, therefore, that the decrease in seven-minute hydrolyzable phosphate during the course of life, which occurs after the fashion of an exponential function, can be attributed above all to the variation in the proportion of the weight of the nucleus to that of the cortex.

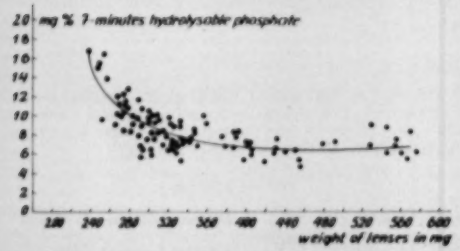


Fig. 15 (Müller, et al.). Dependence of the content of seven-minute hydrolyzable phosphate on the weight of rabbit lenses.

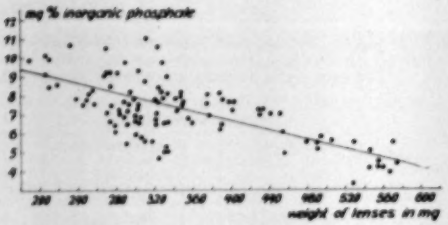


Fig. 16 (Müller, et al.). Dependence of the content of inorganic phosphate on the weight of rabbit lenses.

These results show that for the purpose of solving many of the questions, the investigation of individual parts of the lens is more valuable than an investigation of the lens as a whole. Kinsey and Nordmann have already acted extensively on this basis.

We are indebted to Nordmann and Mandel (1952a) for very detailed investigations into the behavior of the individual phosphoric acids in the lens as the subject gets older.

From their results, which are set out in Table 5, it can be seen that all the phosphoric esters investigated suffer a more or less marked decrease. The striking fact is that this decrease is not uniformly distributed over the various esters. For instance, the content of ATP + ADP and that of phosphagen in the cattle lens falls by about 36 and 48 percent, respectively, whereas hexose diphosphate and glucose-6-phosphate only suffer a decrease of 18 percent and 16 percent, respectively. On the other hand, the content of phosphoglyceric acid again shows a decrease of 46 percent.

These differences cannot be attributed to the cortex and nucleus behaving differently as regards the content of these esters, because it will be seen from Table 5 that all the phosphoric esters in the cattle lens decrease by approximately the same percent-

age in the nucleus as in the cortex. It is only the inorganic phosphate which behaves differently in this respect.

Differences in the percentage decreases brought about by age in the individual phosphoric esters cannot therefore be entirely due to the fact that the carbohydrate metabolism of the lens becomes more restricted in scope as life goes on, but there must also be some change in the actual course such metabolism follows. It could well be, for instance, that the ratio of the amount of glucose catabolized glycolytically and that catabolized oxidatively suffers a change as a result of age. However, it would also be possible as life proceeded for use to be made to a larger or lesser extent of the bypaths of carbohydrate catabolism. In this connection, what is referred to as the hexose monophosphate shunt comes to mind. Nordmann (1954) has provided proof of this process taking place in the lens. Dische, Muñoz, Ehrlich and von Sallmann (1953) believe that this shunt plays a part in the capsule of the lens. In the last resort we can also envisage the possibility that the difference in the decrease in the individual phosphoric esters during the course of life is due to differences in the decrease because of age in the activity of the various enzymes.

Thus it has been ascertained that as cattle get older there is a decrease in the activity of the hexokinase (Süllmann, 1937a; Müller, 1937b) and the aldolase (Müller, 1937b) in the lens, while the glycerophosphatase shows no difference due to age. These observations were confirmed in 1938 by Santoni in respect to phosphatase and in 1941 by Milano in respect to hexokinase.

It is not, however, only the different percentage decrease with age in the various phosphoric esters in the lens which point to the fact that the carbohydrate metabolism in the lens of young animals follows a different course from that in old animals, but the same point is indicated by our investigations regarding the way in which the P^{32} which permeates into the lens is distributed to the various phosphate fractions.

Müller and Kleifeld (1952b) were able to demonstrate that lenses of older animals possess a smaller capacity for the active absorption of phosphate than those of younger animals. This can be seen from the figures given in Table 22. In addition they established that the radioactive P^{32} which passed into the lens was distributed among the various phosphate fractions in a different way in the case of older animals than in the case of younger animals. The electrophoresis graphs reproduced in Figures 12 and 17 show this difference very clearly.

The planimetric evaluation of these graphs, as shown in Table 23, showed that the dif-

TABLE 22

COUNTS PER MINUTE PER GM. LENS IN PERCENT OF COUNTS PER MINUTE PER ONE CM.³ BATH SOLUTION FOR P^{32}

Lenses of Young Rabbits Weighing Up to 0.349 gm.					Lenses of Older Rabbits Weighing Above 0.450 gm.				
Time of Incubation	Number of Experiments	Average Weight of Lenses (in gm.)	P^{32} Uptake in %	σ_M	Time of Incubation	Number of Experiments	Average Weight of Lenses (in gm.)	P^{32} Uptake in %	σ_M
1	15	0.2864	26.6	± 1.4	1	2	0.4629	22.4	±0.4
2	16	0.2561	52.8	± 2.6	2	10	0.5400	26.1	±5.0
4	23	0.2313	96.7	± 4.1	4	17	0.5433	51.8	±2.7
6	12	0.2717	131.7	±10.0	6	10	0.5916	80.1	±5.1
8	6	0.300	144.2	± 6.8	8	8	0.5535	72.3	±4.2

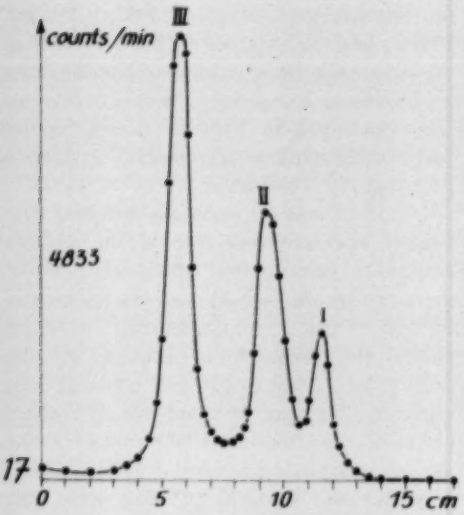


Fig. 17 (Müller, et al.). P^{32} distribution after separation by paper electrophoresis of an aqueous extract of the lens of an old rabbit.

ference caused by age in the incorporation of P^{32} occurs principally in the case of the "residual phosphate." While about 19 percent of the P^{32} which penetrated into the lens was found in the "residual phosphate fraction" in the case of younger animals, this proportion rises to 31 percent in the case of older animals. This increase is almost entirely due to the fact that less P^{32} is present in the inorganic phosphate fraction in the lenses of older animals than in younger ones. Both with younger animals and older animals we find that about 50 percent of the P^{32} which has penetrated the lens is in the ATP.

Differences of this sort cannot be just due to less glucose being catabolized in the lenses of older animals. It is more likely that they are the result of changes in the carbohydrate catabolism. The knowledge of this fact seems to us to be of importance, because it shows us the way to take if we wish to obtain a further elucidation of the changes produced by age in the phosphate metabolism of the lens.

In view of the fact that, under the experimental conditions which obtained, the phosphate metabolism was only investigated in the superficial layers of fibers in the lens, the cause of the differences found must be sought in processes which take place in the superficial strata of the lens.

Phosphate metabolism of the cataractous lens

From numerous investigations which have been carried out, we know that the various types of cataract formation are bound up with disturbances in the sugar metabolism. Nordmann has dealt with this subject exhaustively in his monograph *Biologie du Cristallin*.

A decrease in the glucose content of the lens has been found in the case of senile cataract in man (Lottrup-Andersen, 1927; H. K. Müller, 1934; Salit, 1944), in experimental complicated cataract (Auricchio, 1949) and in cataract due to tryptophane deficiency (Berardinis, 1949). An increase of the sugar content is only reported by Bellavia and Mirto (1935) in cases of experimental traumatic cataract.

TABLE 23

P^{32} distribution in percent among the phosphate compounds, which were separated by paper electrophoresis, of lenses of young and old rabbits after four hours' incubation in a bath solution containing P^{32}

Number of Experiments	Average Weight of Lenses (in gm.)		Inorganic Phosphate		ATP		"Residual Phosphate"	
31	0.286	young	28.1	±1.33	52.8	±0.76	19.1	±0.93
11	0.556	old	18.0	±1.8	51.1	±1.0	30.9	±1.0
			−10.1		− 1.7		+11.8	

Traumatic cataract and experimental complicated cataract would appear to go hand in hand with a decrease in the sugar consumption while galactose cataract and naphthalene cataract show an increased sugar consumption in their early stages.

The investigations of Auricchio (1949) into complicated cataract and those of Müller (1939b) into naphthalene cataract have shown an increase in the lactic acid content. In these cases of cataract the production of lactic acid is increased during the initial stages (Müller, 1939b; Nordmann, Zimmer, and Mandel, 1952) and then decreased at a later period (Nordmann, Zimmer, and Mandel, 1952). Cataract which follows the removal of the parathyroid glands and also that following tetany caused by calcium deficiency of the food, as well as irradiation cataract, cataract due to tryptophane deficiency, massage cataract, cataract caused by anoxemia, galactose cataract, and senile cataract are all accompanied by a decrease in the production of lactic acid.

F. P. Fischer (1938) demonstrated that there was a decrease in the pyruvic acid content in senile, congenital, myotonic, complicated (Auricchio-Ambrosio, 1953) and traumatic cataract.

From these findings it is quite clear that many forms of lens clouding are connected with disorders in the carbohydrate metabolism. Unfortunately, the experimental results at present available are not such as to make it possible to make a definite pronouncement as to whether the disturbances in the carbohydrate metabolism are similar or different for the various types of lens clouding.

Disturbances in the phosphate metabolism in the diseased lens have also been observed, which correspond with these changes in the carbohydrate metabolism. It is not necessary for us to go into greater detail regarding the various results obtained in this respect, because we can draw no special conclusions from them as yet.

Nevertheless, the results obtained by Nordmann and Dillschneider (1951), Nordmann, Mandel, and Achard (1953), and also by Achard (1954) are worthy of note. In series of experiments in vitro these authors have interrupted the carbohydrate metabolism of the lens at various points, using glyceraldehyde, iodine monoacetic acid, phlorizin, sodium fluoride, fluoroacetate, and sodium malonate. Under these conditions they found that the ATP content is decreased in all lenses. In the experiments using iodine monoacetic acid the phosphagen content was also determined and was found to be greatly reduced. The inhibitors which act in the initial stages of carbohydrate catabolism, namely, glyceraldehyde, iodine monoacetic acid, phlorizin, and sodium fluoride, also brought about a decrease in the lactic acid content. In all these experiments there was a comparatively rapid occurrence of lens clouding, and in every case the clouding was preceded by a decrease in the ATP content.

We must, however, also stress the results which have been obtained in cases of the occurrence of cataract caused by naphthalene, galactose (alloxan) diabetes, dinitrophenol, and X-ray irradiation.

From the researches of von Sallmann and Locke (1951) we know that in the case of irradiation cataract disturbances are only found in the phosphate metabolism after the clouding of the lens has proceeded a comparatively long way. Under these circumstances there is a decrease in the amount of P^{32} taken up by the cataractous lens and this is then distributed more or less uniformly throughout the entire lens, while in a normal lens it is found almost exclusively in the marginal zones. Nordmann, Mandel, and Achard (1953) were able to show no disturbance of the sugar or phosphate metabolism in the transparent lens after X-ray irradiation.

In the case of galactose cataract, Nordmann and Mandel (1953) found a decrease in the ATP content and also in the proportion of the easily hydrolyzed phosphate

of the ATP to the nucleotide phosphate, even before the first signs of clouding in the lens occurred. They also reported a decrease in the phosphagen content.

The authors cited also obtained exactly the same results in the case of diabetic cataract brought about by alloxan.

Contrary to these results, Nordmann and Mandel (1952c) found only a slight change in the intermediate products of carbohydrate metabolism in the case of naphthalene cataract. When reporting these results they stated that the ratio of easily hydrolyzed phosphate of the ATP to nucleotide phosphate, which is normally 1.63 to 1.85, had decreased to 1.47 to 1.50.

These investigations already show quite clearly that there are considerable differences in the course followed by the carbohydrate metabolism in cases of lens damage through X-ray irradiation, galactose, alloxan diabetes, and naphthalene.

We can confirm this on the basis of our own researches. We thus found, as Table 24 shows, that 24 hours after the administration of naphthalene the intake of P^{32} into the lens was hardly affected. However, when the rabbits were given naphthalene again 48 hours after the first administration of this chemical and the lenses investigated 24 hours after that, a decrease was discernible in the capacity to take up P^{32}. The seven-minute hydrolyzable phosphate content was slightly reduced.

A striking fact was that we could ascertain no disturbance in the percentage distribution of the P^{32} over the three fractions into which the phosphates can be separated by electrophoresis, in spite of the disturbance in the absorption and in spite of the slight decrease in the quantity of seven-minute hydrolyzable phosphate. The transparent and clouded lenses of the animals on a naphthalene diet showed no noticeable differences in these investigations of the phosphate metabolism.

There was a different behavior on the part of the lenses of rabbits in which we had induced diabetes by means of a single intravenous injection of alloxan.

With the methods adopted by us, it was not possible to find any disturbance of the phosphate metabolism 24 hours after the administration of the alloxan. By one week after the administration of alloxan, however, and also 14 weeks later, we found changes in the phosphate metabolism. These were equally noticeable in both the transparent and clouded lenses of the diabetic animals. They consisted in a distinct disarrangement of the percentage distribution of P^{32} into the various phosphate fractions.

Table 25 shows that, both with the younger and older rabbits, this disarrangement made itself felt principally in that as a result of the diabetes there was more P^{32} contained in what is known as the "residual phosphate," that is to say the phosphate which is for the greater part difficult to hydrolyze. Corresponding to this relative increase, there is a decrease of approximately the same magnitude in the ATP.

Generally speaking, the penetration of P^{32} from the nutrient solution into the lens was not appreciably altered. Only in the case of the lenses of quite young animals of one

TABLE 24

P^{32} UPTAKE IN PERCENT, AND P^{32} DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS AND THE CONTENT OF INORGANIC PHOSPHATE AND SEVEN-MINUTE HYDROLYZABLE PHOSPHATE OF THE LENSES OF NORMAL AND NAPHTHALENE-FED RABBITS, AFTER INCUBATION IN A BATH SOLUTION CONTAINING P^{32} FOR TWO HOURS

Number of Feeding-Times	Number of Experiments	Average Weight of Lenses (in gm.)	P^{32}-Uptake in %	P^{32}-Distribution in % Among			Averages in mg. %	
				Inorganic Phosphate	ATP	"Residual-Phosphate"	Inorganic Phosphate	7-min. Hydrolysable Phosphate
Normal	16	0.303	33.5±2.69	15.9	54.8	29.3	8.52±0.2	9.86±0.44
1×	12	0.282	30.8±2.3	19.1	54.2	26.7	9.70±0.4	7.55±0.4
2×	22	0.343	23.4±1.29	13.7	52.0	34.3	8.39±0.3	7.50±0.6

TABLE 25

P^{32} DISTRIBUTION AMONG THE DIFFERENT PHOSPHATE COMPOUNDS OF THE LENSES OF NORMAL AND DIABETIC RABBITS

Normal Rabbits					Diabetic Rabbits by Alloxan				
Number of Experiments	Average Weight of Lenses (in gm.)	P^{32} Distribution in % Among			Number of Experiments	Average Weight of Lenses (in gm.)	P^{32} Distribution in % Among		
		Inorganic Phosphate	ATP	"Residual-Phosphate"			Inorganic Phosphate	ATP	"Residual-Phosphate"
31	0.286	28.1±1.33	52.8±0.76	19.1±0.93	23	0.351	29.5±2.4	38.9±1.43	31.6±2.28
8	0.579	19.4±1.8	49.4±1.03	31.2±1.08	5	0.552	20.8±7.2	37.9±2.2	41.3±5.1

certain breed and in the case of a few lenses which had suffered particularly severe clouding was there a decrease in the P^{32} absorption.

In a final series of experiments we added 0.25 percent 2,4-dinitrophenol (sodium salt) to the standard food of some chicks about two weeks old. Without exception there was clearly discernible clouding in the lenses after only six hours. At this juncture, however, we were not able to ascertain any disturbance to the phosphate intake into the lens or any change in the distribution of the P^{32} over the various phosphate fractions. Furthermore, there was no deviation from the normal content of inorganic phosphorus and seven-minute hydrolyzable phosphate in the lens. It was not possible by our methods to discern any disturbance of the phosphate metabolism in these lenses.

We can see, therefore, that the effect on the phosphate metabolism is different in the case of naphthalene poisoning (decreased P^{32} absorption, no disturbance of the process of incorporation in the phosphate fractions we tested and a slight decrease in the content of seven-minute hydrolyzable phosphate), in the case of alloxan diabetes (no special decrease in the P^{32} absorption but a distinct change in the way it is incorporated into the various phosphate fractions), and in the case of dinitrophenol poisoning (no disturbance of the phosphate absorption, no disturbance of the process of incorporation, no disturbance in the content of seven-minute hydrolyzable phosphate).

We believe that by this report we have been able to show that an investigation of the phosphate metabolism offers great promise in regard to increasing our knowledge of the physiology and pathology of the crystalline lens.

University Eye Clinic.

References

Achard, M.: Diss. inaugur. Cited by Nordmann, J., 1954.

Adams, D. R.: Proc. Roy. Soc. London, B, **98**:244, 1925.

Ahlgren, G.: Acta ophth., **5**:1, 1927.

Ames, S. R., and Elvehjem, C. A.: Arch. Biochem., **10**:443, 1946.

D'Asaro, B. S., Young, R. G., and Williams, H. H.: Arch. Ophth., **51**:596, 1954.

Auricchio, G.: Ann. ottal. e clin. ocul., **75**:89, 1949.

Auricchio, G., and Ambrosio, A.: Giorn. ital. oftal., **6**:489, 1953.

Bellavia, A., and Mirto, E.: Boll. ocul., **14**:823, 1935.

Berardinis de, E.: Giorn. ital. oftal., **2**:350, 1949.

———: Atti Soc. oftal. ital. Cited by Nordmann, 1954, p. 165.

Berardinis, de, E., and de Rosa, L.: Atti Soc. oftal. ital., 1952. Cited by Nordmann, 1954.

Boyland, E.: Biochem, J., **22**:362, 1928. Cited by Krause, A. C., and Weekers, R.: Arch. Ophth., **20**: 302, 1938.

Brolin, S. E., and Nordström, E.: Acta anat., **14**:1, 1952.

Brückner, R.: Ophthalmologica, **100**:203, 1940.

Chernick, S. S., Chaikoff, J. L., and Abraham, S.: J. Biol. Chem., **193**:793, 1951.

Christiansen, G. S., and Leinfelder, P. J.: Am. J. Ophth., **35**:11, 21, 1952.

Christianssen, J., and Palm, E.: Acta Ophthal., **32**:197, 1954.

Cristini, G., and Cuisa, W.: Ann. ocul., **180**:742, 1947.

Corrado, M.: Giorn. ital. oftal., **3**:248, 1950.
Daily, L., Zeller, E. A., Wakim, K. G., Herrick, J. F., and Benedict, W. L.: Am. J. Ophth., **34**:1301, 1951.
Dische, Z.: Reported at the 1st Internat. Cong. Biochem., Cambridge, 1949. Cited by Dische, Z.: Phosphorus Metabolism. Baltimore, Johns Hopkins Press, 1951.
———: Cited by Sallmann, von, L., and Locke, N. D.: 1951.
Dische, Z., Ehrlich, G., Munoz, C., and von Sallmann, L.: Am. J. Ophth., **36**:54 (June, Pt. II), 1953.
Ely, L. O.: Am. J. Ophth., **32**:220, 1949.
———: Am. J. Ophth., **34**:127, 1951.
Ely, L. O., and Robbie, W. A.: Am. J. Path., **33**:269, 1950.
Euler, von H., and Günther, G.: Ztschr. physiol. Chem., **256**:229, 1938.
Euler, von H., Hellström, H., Schlenk, F., and Günther, G.: Arch. f. Ophth., **140**:116, 1939.
Evans, E. J., and Kern, R.: Am. J. Ophth., **14**:1029, 1931.
Felix, K.: Naturwissenschaften, **40**:44, 1953.
Fischer, F. P.: Arch. Augenh., **107**:295, 1933.
———: Arch. Augenh., **109**:468, 1936.
———: Arch. Ophth., **2**:108, 1938.
———: Ophthalmologica, **114**:1, 1947.
François, J., and Rabaey, M.: Ann. ocul., **184**:481, 1951.
Friedenwald, J. S.: Arch. Ophth., **3**:182, 1930.
Frohman, C., and Kinsey, V. E.: Arch. Ophth., **48**:12, 1952.
Giörgy, P.: Biochem. J., **29**:760, 1935.
Goldschmidt, M.: Ber. deutsch. ophth. Gesellsch., **44**:137, 1924.
Herrmann: Ztschr. f. wissenschaftl. Mikroskopie, **49**:313, 1932.
Herrmann, H., and Moses, S. G.: J. Biol. Chem., **158**:47, 1945.
Hevesy, G.: Am. Rev. Biochem., **9**:641, 1940.
Heyningen, van R., and Pirie, A.: Biochem. J., **53**:436, 1953.
Horecker, B. L.: In Phosphorus Metabolism, Baltimore, Johns Hopkins Press, 1951.
Hunter, F. E., Jr.: J. Biol. Chem., **177**:361, 1949. (a)
———: J. Biol. Chem., **181**:67, 1949. (b)
Kaganiya, A.: Vestnik. Oftal., **30**:33, 1951 cited by Nordmann 1954.
Kalkar, H. M.: J. Biol. Chem., **158**:723, 1945.
Kinsey, V. E., and Frohman,C. E.: Arch. Ophth., **46**:536, 1951.
Kinsey, V. E., and Merriam, F.: Arch. Ophth., **44**:370, 1950.
Kleifeld, O.: Arch. f. Ophth., **154**:332, 1953.
Kleifeld, O., Fuchs, R., Hockwin, O., and Arens, P.: Ber. deutsch. ophthal. Ges., **58**:220, 1953.
Kodicek, E.: Biochem. J., **34**:724, 1940.
Koller, S.: Graphische Tafeln zur Beurteilung statistischer Zahlen. Dresden und Leipzig, Steinkopf, 1940.
Krause, A. C.: The Biochemistry of the Eye. Baltimore, Johns Hopkins Press, 1934.
———: Arch. Ophth., **13**:187, 1935.
———: Am. J. Ophth., **21**:1343, 1938.
Krause, A. C., and Stack, A. M.: Arch. Ophth., **22**:66, 1939.
Krause, A. C., and Weekers, R.: Arch. Ophth., **20**:299, 1938.
Kronfeld, P., and Bothman, L.: Ztschr. f. Augenh., **65**:41, 1928.
Lang, K.: Der intermediäre Stoffwechsel. Heidelberg, 1952.
Leber, A. T.: Arch. f. Ophth., **62**:85, 1906.
Leinfelder, P. J., and Christiansen, G. S.: Am. J. Ophth., **35**:33 (May, Pt. II) 1952.
Leonibus, de: Rassegna ital. ottal., **10**:547, 1941. Cited by Nordmann, 1952.
Lo Cascio, G.: Ann. di ottal., **50**:219, 1922.
Lodato, G.: Arch. ottal., **13**:318, 1905.
Lohmann, K.: Bioch. Ztschr., **194**:306, 1928.
Lottrup-Andersen, C.: Acta Ophth., **5**:226, 1927.
Lüderitz, B.: Klin. Monatsbl. f. Augenh., **99**:75, 1937.
Lynen, F., and Reichert, E.: Angew. Chem., **63**:47, 1951.
Lynen, F., and Holzer, H.: Liebigs Ann. Chem., **563**:213, 1949.
Lynen, F., Reichert, E. and Rueff, L.: Liebigs Ann. Chem., **574**:1, 1951.
Mackay, G., Robertson, C. P., and Robertson, J. D.: Brit. J. Ophth., **16**:193, 1932.
Mandel, P., and Israelewicz, D.: Cited by Nordmann, 1954.
Mandel, P., and Klethi: Cited by Nordmann, 1954.
Mandel, P., Nordmann, J., and Zimmer, J.: Cited by Kinsey, V. E.: Arch. Ophth., **44**:596, 1950.
Mandel, P., Nordmann, J., Zimmer, J., and Harth, S.: Nature, **164**:794, 1949.
Mandel, P., and Zimmer, J.: Compt. rend. Soc. biol., **146**:762, 1952.
Martius, C.: Colloq. Ges. f. physiol. Chem., Moosbach, 1954.

Milano, A.: Ann. ott. e Clin. ocul., **69**:175, 1941.
Mishima, J.: Acta Soc. Ophth. Japan, **56**:76, 1952.
Müller, H. K.: Ber. Versamml. deutsch. ophth. Gesellsch., **50**:167, 1934.
———: Arch. Augenh., **109**:434, 1936 (a).
———: Arch. Augenh., **109**:497, 1936 (b).
———: Arch. Augenh., **110**:321, 1937 (a).
———: Arch. Augenh., **110**:206, 1937 (b).
———: Arch. Augenh., **110**:128, 1937 (c).
———: Ber. Versamml. deutsch. ophth. Gesellsch., **52**:300, 1938.
———: Arch. f. Ophth., **140**:171, 1939 (a).
———: Arch. f. Ophth., **140**:258, 1939 (b).
Müller, H. K., and Kleifeld, O.: Klin. Woch., **30**:662, 1952 (a).
———: Arch. f. Ophth., **153**:177, 1952 (b).
———: Arch. f. Ophth., **154**:165, 1953 (a).
———: Ber. Versamml. deutsch. ophth. Gesellsch., **58**:14, 1953 (b).
Müller, H. K., Kleifeld, O., Arens, H. P., Dardenne, U., Fuchs, R., and Hockwin, O.: To be published.
Nordmann, J.: Biologie du Cristallin. Paris, 1954.
Nordmann, J. and Dillschneider, L.: Bull et mém. Soc. franç. ophtal., **64**:122, 1951.
Nordmann, J., and Mandel, P.: Ann. d'ocul., **185**:929, 1952 (a).
———: Compt. rend. Acad. sci., **235**:834, 1952 (b).
———: Bull. Soc. belge d'ophtal., **102**:524, 1952 (c).
———: Comp. rend. Acad. sci., **236**:426, 1953.
Nordmann, J., Mandel, P., and Achard, M.: Cited by Nordmann, 1954.
Nordmann, J., Zimmer, J., and Mandel, P.: Comp. rend. Soc. Biol., **146**:1804, 1952.
O'Brien, C. S., and Salit, P. W.: Am. J. Ophth., **14**:582, 1931.
Palm, E.: Acta Ophth. Suppl., 1948, p. 32.
———: Acta Ophth., **32**:49, 1954.
Philpot, F. J., and Pirie, A.: Biochem. J., **37**:250, 1943.
Pignalosa, G.: Ann. ottal. e clin. ocul., **67**:927, 1939 (a).
———: Boll. Ocul., **18**:646, 1939 (b).
———: Boll. Ocul., **23**:243, 1944.
Rizzo, A.: Boll. Soc. ital. biol. sper., **12**:810, 1937 (a).
———: Boll. Soc. ital. biol. sper., **12**:813, 1937 (b).
Rochat, G. F.: Klin. Monatsbl. f. Augenh., **103**:432, 1939.
Ross, E. J.: Nature, **171**:125, 1953.
Salit, P. W.: Brit. J. Ophth., **19**:663, 1935.
———: Arch. Ophth., **16**:271, 1936.
Salit, P. W., Swan, K. G., and Paul, W. D.: Am. J. Ophth., **25**:1482, 1942.
Salit, P. W.: Arch. Ophth., **30**:255, 1943.
Salles, I. B. V., and Ochoa, S.: J. Biol. Chem., **187**:849, 1950.
Sallmann, L. von and Locke, J. C.: Arch. Ophth., **45**:431, 1951.
Santoni, A.: Ann. ottal. e clin. ocul., **66**:208, 1938.
Sauermann, A.: Am. J. Ophth., **16**:985, 1933.
Schild, K. T., and Maurer, W.: Biochem. Ztschr., **323**:235, 1952.
Schlenk, F., and Waldvogel: Arch. Biochem., **12**:181, 1947.
Schmid, A. E. and Bürki, E.: Ophthalmologica, **105**:65, 83, 1943.
Simonelli, M.: Boll. ocul., **20**:163, 1941.
Stetten, M. R. and Stetten, D. W., Jr.: J. Biol. Chem., **164**:85, 1946.
Süllmann, H.: Arch. Augenh., **110**:303, 1937 (a).
———: Klin. Wchnschr., **45**:1583 (II) 1937 (b).
———: Tabul. biol., **22**:161 (II) 1951.
Updegraff, H.: Proc. Soc. Exper. Biol. & Med., **29**:964, 1932.
Walaas, E., and Walaas, O.: J. Biol. Chem., **195**:367, 1952.
Weekers, R.: Arch. Ophthal., **1**:707, 1937.
———: Soc. Belge d'ophtal., **79**:44, 1940.
———: Thése d'agrégation, Liége, 1941.
Weekers, R. and Süllmann, H.: Arch. internat. Med. exp., **13**:483, 1938.
Zimmer, J., Mandel, P., and Nordmann, J.: Compt. rend. Soc. biol., **146**:1795, 1952.

Discussion

Dr. P. J. Leinfelder (Iowa City): It is with a great deal of humility that I begin the discussion of this paper. I had an opportunity to read it and I was impressed by the completeness of the work and the thoroughness of the bibliography. The way in which the various problems were approached

and solved was masterful. Dr. Müller has covered the theory of metabolism of the lens and cataract. He has brought to our attention the many facts, past and present, involved in a study of the metabolism of the lens. He has pointed the way to those who are separated from us and seem to minimize the place of metabolism in the function of the lens. He has clearly outlined why metabolism is necessary in the function of the lens and has shown the effects of that metabolism, as it can be studied through observing the production of triphosphates that are so important in storing the energy that is produced by glycolysis or respiration. He has illustrated by experiments the relative importance of glycolysis and respiration in the metabolism in the lens and showed how this is reflected in the phosphate balance and that the function of triphosphate is definitely associated with the metabolic activity of the lens.

We, of course, have been very much interested, too, in the functional activity of the lens and my associates, Dr. Schwartz in particular, have been active in research to demonstrate the role of metabolism in water transport. To those of us who believe in active transport there is a relationship between the metabolism and the maintenance of a status quo of the lens—maintenance that is demonstrated by a study of the water balance or ion exchange or the synthesis of protein or the utilization of phosphorus. The relative roles of respiration and glycolysis are not clearly established, although it can be shown that movement of water in and out of the lens, the active transport of water, is dependent upon the metabolic activities. If we depress respiration with cyanide or glycolysis by absence of glucose or with iodoacetic acid, we find that the water transport is inhibited and the lens swells but the swelling can be reversed when the metabolism is re-established. The same thing applies when the cornea is used as the experimental tissue.

Glycolysis is said to be a very inefficient method of obtaining energy, but that is true only to a certain extent. Glycolysis does not break glucose into carbon dioxide and water, and the statement saying that glycolysis is inefficient is based on the fact that the energy obtained from glycolysis is only that which occurs from the break-down of glucose to lactic acid. There is a lot of energy left in the lactic acid and this is liberated when the lactic acid is converted to pyruvic acid and enters the respiratory cycle where it is broken down to carbon dioxide and water.

Some tissues can survive for a long time on energy produced by glycolysis, and although we do not feel that one should or can say that respiration plays no part in the metabolism of the lens, we feel that glycolysis is one source of its energy production and that any respiration that occurs is perhaps related to the growth and maintenance or the epithelium.

I think that we should continue to bear in mind the nonenzymatic processes that we demonstrated a number of years ago: the oxygen uptake that occurs with the boiled lens, which is of the same magnitude as the oxygen consumption of the unboiled lens. This nonenzymatic oxygen uptake is also cyanide sensitive. Also, although there has been extensive literature on the role of ascorbic acid and glutathione in the metabolism of the lens, we are still without basic information concerning just where they enter into the metabolic picture. However, it appears that the nonenzymatic oxygen uptake of the lens is due to the oxidation of glutathione and ascorbic acid which is catalyzed by a heavy metal that can be taken out of its catalytic role by the cyanide.

The information gained through Dr. Müller's work and other research presents the simplifications to make oversimplifications. We perhaps have been involved in that enough previously. I think we who are doing work on the fundamental physiology of the lens and the cell must guard against narrow conclusions. It is important that we be broad in our knowledge so that we take into consideration all points of view, all circumstances, and all the phenomena involved. I think the errors that we make are due to taking a single experiment and interpreting it too broadly. I suggest that perhaps in a discussion of experimental cataracts one could do that. Isn't it a mistake to compare directly the morphogenesis and the pathogenesis of diabetic cataract and X-ray cataract? Although having certain relationships, they are not the same.

Radiation cataract is due to an ionizing effect, the precise nature of which is unknown, but perhaps involves the lens epithelium cells in such a way that after a prolonged period, the effect becomes manifest.

In the diabetic cataract we have an injury to the cells due to interference with glucose metabolism. We know that glucose is a primary source of energy for the lens. We know that in the diabetic there is interference with phosphorylation. The result of the diabetes, if of sufficient severity, is that of a deprivation of substrate, and often the injury occurs at the time diabetes is in its incipiency when the metabolic processes were impaired but the cataract is not recognized until several months later. This is similar to the latent period which occurs in X-ray cataract.

I think Dr. Müller's statement that very frequently the lens changes are already present before changes in phosphate uptake are observed is very important. It indicates that we should not assume relationships without having all the facts available.

My discussion has been general. It applies little to Dr. Müller's paper because Dr. Müller has clearly outlined what happens in phosphorus metabolism under (a) normal metabolism, (b) when metabolism is inhibited, (c) in the aging process, and (d) when cataract develops.

In addition, he has shown that there is a relationship between the metabolic activity and the production of high energy phosphate, and that is

so because the lens is a living structure that has a function that requires energy for its growth and maintenance. High energy phosphorus provides that energy to keep the lens clear, to allow for the growth of the epithelium of the lens, and to permit the numerous synthetic processes that must take place in order to keep it alive.

DR. MÜLLER (Bonn, Germany): I wish to thank Dr. Leinfelder for his comment and his discussion. It was very interesting to hear that he has also investigated the water transport into the lens and that he, too, found that this depends on an active transfer. I think that this is of great importance as water is the main constituent of the lens. It was interesting to hear that Dr. Leinfelder believes that glutathione and ascorbic acid and their oxidation and reduction influence the cyanide-sensitive processes near the posterior surface of the lens. I also think that it is important to consider the results obtained by Dr. François on the electrophoretic pattern of lens globulins at various ages and with cataract formations.

CRITICAL FLICKER FREQUENCY IN AMBLYOPIA EX ANOPSIA*

IRWIN FEINBERG, M.D.
Boston, Massachusetts

INTRODUCTION

Amblyopia ex anopsia is a familiar clinical condition, but the nature of this visual aberration remains obscure. Until recently, the amblyopia was considered primary and due to structural defect, the squint being a secondary response to the amblyopia. Currently, the reverse is believed to be true: the ocular deviation is primary, and the amblyopia develops as a by-product of some complex adaptive process whose principal function is to prevent diplopia.

Investigating the dimensions of visual function that are altered in amblyopia ex anopsia, Wald and Burian (1944) found that dark adaptation, spectral sensitivity, and absolute brightness threshold were equal in normal and amblyopic eyes. On this basis, and on the basis of their interpretation of ablation experiments in subhuman mammals, they concluded that the "entire apparatus of light perception" is normal in the affected eye, and that depression of acuity is attributable to selective impairment of a "higher" visual function—that of pattern vision.

This interpretation has gained acceptance in standard texts of ophthalmology (Duke-Elder, 1949; Walsh, 1947). A similar selective impairment has been claimed to exist in visual agnosia. The classical definition of this syndrome requires that the highest visual function (recognition) be lost, while response to the elementary aspects of visual stimulation remains intact. These two conditions, amblyopia ex anopsia and visual agnosia, represent the prime examples for those who claim that it is possible in vision for a higher function to be seriously deranged without demonstrable impairment on a lower level.

More recent investigations of visual performance after cerebral lesions have, however, revealed deficits which are not demonstrated by routine perimetric and acuity tests. These special investigations disclose such changes as an abnormally rapid fading of contours (Bay, 1953) or lowered flicker fusion (Battersby, 1951). It should be noted that these are tests which tax the visual system by requiring either a prolonged or else a very rapid response. The deficits thus discovered are nevertheless quite real, and may play a role in visual agnosia. Indeed, there are some who claim that all cases of so-called

---

* This study was carried out at the Psychophysiological Laboratory, New York University—Bellevue Medical Center. I am indebted to Dr. H. L. Teuber, head of this laboratory, who suggested this problem, for his guidance and encouragement. I am also indebted to Dr. Sidney Weinstein for his invaluable advice in the statistical treatment of the data.

visual agnosia might show such changes (Bay, 1953). Since such disturbances would be readily classified according to traditional description as being alterations in lower level functions, the classical dissociation implied by agnosia with its hierarchical separation of function is rendered doubtful.

The same questions might be raised by the interpretation which Wald and Burian have given to amblyopia ex anopsia. In their own survey, many basic functions were found intact but the range of tests was necessarily limited. They did not include tests of flicker fusion or of prolonged fixation. We have decided therefore to measure the critical flicker frequency in central and peripheral portions of the field of vision in amblyopia ex anopsia.

The critical flicker frequency (CFF) is defined as that rate of intermittence (in cycles/sec.) above which a light source appears subjectively steady and below which it appears to flicker. Specifically, we postulated that there would be a disturbance of critical flicker frequency in the amblyopic eye which would parallel, in retinal distribution, the depression in acuity. Since most evidence points to the foveal area as the site of the amblyopia (Duke-Elder, 1949), we would expect critical flicker frequency to be altered mainly in this region. Such a finding would argue against the selective impairment of higher as contrasted with lower visual function, and against the anatomico-physiologic separation thereby implied.

For such a study to be effective, control of fixation is essential. Since fixation with the squinted eye may result in projection on an extrafoveal area, one of the objectives of the present study was to devise a method to insure foveal fixation. In brief, the method decided upon consists in maneuvering a luminous target until it disappears in the subject's blindspot. Any shift in gaze will bring this object back into view, alerting the subject to his change in ocular posture. (This technique presupposes, of course, that the anatomic relation between the blindspot and the fovea is roughly constant.)

Such safeguards of fixation were not employed in the two previous investigations of critical flicker frequency in amblyopia ex anopsia. The first study, a dissertation by Teräskeli (1934), showed critical flicker frequency in the normal eye to be higher in the periphery than in the fovea. This difference tended to be obliterated in the amblyopic eye. Miles' study (1949) essentially confirmed Teräskeli's findings, although he could reproduce her fovea-periphery gradient at only one peripheral position. In this laboratory, however, maximum critical flicker frequency in normal eyes has consistently been demonstrated for the fovea, with declining values as one moves peripherally in the temporal or nasal direction.

The existence of such discrepancies and the doubt as to the adequacy of fixation in the previous studies made the present investigation seem necessary. In summary then, our study was undertaken to test, by measuring flicker fusion under conditions of controlled fixation, whether visual disfunction in amblyopia ex anopsia truly represents a dissociation of pattern vision and light perception.

Material and Method

Apparatus

The apparatus employed was that first used by Teuber and Bender (1948), and included the electronic timer added by Battersby (1951). Essentially, this consists of a multivibrator which produces rectangular pulses led into a dummy load. When the subject actuates a microswitch held in his hand, the pulse is switched from the dummy level to the light source which is then exposed for a duration preset on the timer.

The source, a Sylvania tube R 1130 B, is mounted on the arm of a standard Brombach perimeter at the level of the usual fixation point. This apparatus permits accurate control of the following stimulus parameters: (a) frequency, (b) light-dark ratio, (c) duration of exposure, (d) position in the visual field. The first two parameters could be monitored directly on an oscilloscope tube

built into the front panel of the instrument.

The intensity of the light source was constant throughout, approximately 8.91 apparent foot-candles, and the light was of a slightly pinkish hue (maximal emission at 6,000 Å). The light source was reflected on a ground glass screen, the target size was determined by the central aperture of a machined disc interposed between the source and the screen. A more complete description of the apparatus may be found in Battersby (1951).

Four patches of faintly luminous paint, 0.5 cm. in diameter, were placed about the target, each 0.5 cm. from its edge, at positions corresponding to the 12-, 3-, 6-, and 9-o'clock positions. The light-dark ratio was set at 1, the target size at 1.03 degrees. The target was viewed through an artificial pupil provided by a two-mm. aperture in an aluminum shield held in front of the eye.

The fixation target was roughly 0.75 degrees in diameter, and its intensity was maintained by means of a rheostat at the lowest level of brightness compatible with clear fixation. When foveal stimulation was desired, the fixation target was disconnected and the subject fixated the point at the center of the four luminous spots.

The blindspot patch was a spot of luminous paint, varying in size from one to two degrees of visual angle, mounted on a freely movable stand at the height of the fixation and flicker sources. All light sources were maintained on a single horizontal meridian. The distance from the eye to these targets was 260 mm.

Subjects

The subjects were nonhospitalized adults with long-standing cases of uniocular squint. They were selected according to the following criteria: (a) acuity depression in the deviated eye to or below 20/100 Snellen which could not be improved by refraction, (b) absence of diplopia in everyday life, (c) absence of ophthalmoscopic abnormality. Three subjects met these criteria. A fourth subject, who differed in that she experienced frequent diplopia, was also tested. The age, clinical history, and Snellen acuity of these subjects will be found in the Appendix.

Six normal adults served as controls. Some had depressed acuity secondary to myopia and astigmatism correctible by refraction. An equal proportion of males and females were tested in each group, and the two groups were of comparable ages. Ages and Snellen acuity for the control subjects are listed in the Appendix.

Procedure

All subjects were tested without glasses. The eye not being tested was covered with a standard black eyepatch, the edges being sealed with adhesive tape.

A. *Amblyopic subjects.* The central fields and blindspot were mapped campimetrically with a one-degree white target. One subject (Case 3) was unable to fixate sufficiently with her deviated eye to permit complete mapping. The subjects were then made familiar with the apparatus. The chinrest was adjusted and the room darkened. The techniques of exposing the flicker source by depressing the microswitch, and of viewing the field through the artificial pupil were practiced. The subject was shown the various gradations of coarse and fine flicker.

To ensure steady fixation and therefore stimulation of desired retinal areas, the blindspot patch was placed in the region of the previously mapped blindspot so that it was not seen when forward fixation was maintained. If fixation faltered, and the gaze shifted, the patch became visible. Thus alerted, the subject would resume fixation and repeat the trial.

One subject (Case 3) was not able to maintain fixation for the prolonged period required by this technique. This was the same subject in whom the blindspot could not be mapped adequately. In her case, the experiment was carried out in the following manner: the subject fixated and exposed the flickering source. If she was aware that her eye had moved during the one second exposure of the target, she would repeat the

TABLE 1

MEAN CRITICAL FLICKER FREQUENCY AT EACH RETINAL POSITION OF EACH EYE OF CONTROLS

Control Subject	Left Eye				Right Eye			
	24°T	8°T	0°	8°N	24°T	8°T	0°	8°N
1	15.2	18.2	23.4	15.6	16.6	17.0	26.7	16.0
2	14.7	15.0	23.9	16.2	14.8	16.5	24.6	15.9
3	14.5	15.3	25.8	15.1	14.9	14.5	25.3	14.6
4	16.2	19.3	26.8	16.1	16.2	18.6	22.9	16.5
5	16.9	16.6	27.3	15.8	15.8	17.9	29.2	17.3
6	16.8	17.1	25.9	18.1	15.5	18.0	26.3	16.7
Mean	15.7	16.9	25.9	16.2	15.6	17.1	26.3	16.2
Range	14.5–16.9	15.0–19.3	23.4–27.9	15.1–18.1	14.8–16.6	14.5–18.6	22.9–29.2	14.6–17.3

trial. The subject was extremely conscientious and accepted an average of only one trial in four. Although we cannot be certain, it seemed likely that direct forward fixation resulted in foveal projection since, under this condition, the campimeter target tended to disappear in the region of 13 to 15 temporal from the fixation point.

Critical flicker frequency was determined by the method of limits. The flicker-generator was the first set at a rate of 8 to 10 cycles/sec. below the expected fusion zone, and then increased in steps of 0.25 to 0.5 cycles/sec. after each individual trial. A trial was determined by the subject actuating the microswitch, exposing the stimulus for one second, and then making a judgment. When the light appeared steady, the subject ceased exposing it and said "now." This value was recorded, the rate set at 8 to 10 cycles/sec. above this reading, and decreased in similar steps until the subject noted the first appearance of flicker. In this manner, six determinations (three ascending and three descending) were taken for each retinal position. The subjects were encouraged to repeat exposures at a regular rate, approximately 1/sec. and to rest whenever necessary.

Critical flicker frequency was determined at four positions in each eye. These were tested in the same order in each eye, namely, 24 degrees temporal from the foveal fixation, eight degrees temporal, zero degrees (or foveal), and eight degrees nasal. In half of the group the amblyopic eye was tested first, in the other half, the normal eye.

B. *Control subjects.* The procedure used was identical to the above, except that the central fields were not mapped campimetrically. The blindspot patch was easily introduced into the blindspot by slowly moving it on the same horizontal meridian nasally until it disappeared, after starting at 20 degrees temporal from the fixation point. In half the group, the right eye was tested first, and the left eye in the remaining half.

RESULTS

A. *Controls.* The right and left eyes of the six control subjects are compared in Table 1, which gives the mean critical flicker frequency values for each retinal position. The results are plotted in Figure 1. The close similarity of the two eyes is striking; they do not differ significantly* at any retinal position (table 2). The shape of the curve in Figure 1, with its pronounced peak at the fovea, is quite characteristic of the results previously obtained with this equipment (Battersby, 1951). As may be noted in Table 3, the critical flicker frequency at the fovea is significantly greater than that found at any of the other positions tested.

B. *Amblyopes.* Table 4 lists critical flicker frequency at each retinal position for ambly-

* "t" tests of significance were performed after a complete analysis of variance was carried out.

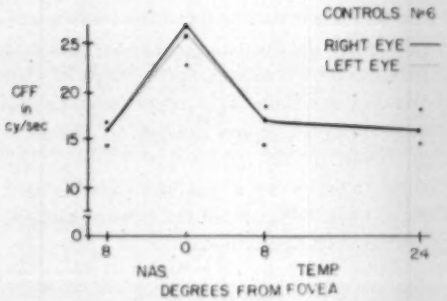


Fig. 1 (Feinberg). Mean critical flicker frequency curves for six control subjects. Black dots above and below curves indicate range for both eyes at each position.

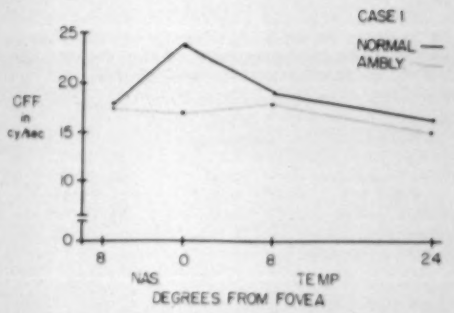


Fig. 2A (Feinberg). Critical flicker frequency curves for Case 1.

opic and normal eyes. Figures 2A, 2B, and 2C show these data. Table 5 lists critical flicker frequency values for Case 4, who did not meet the criteria for inclusion in the amblyopic group. These data are shown graphically in Figure 3.

It may be seen that the curve for the normal eye of the amblyopic group is markedly similar to that of the controls. The mean critical flicker frequency for this eye does not differ significantly from that of the controls at any retinal position. The foveal critical flicker frequency of the normal eye of the amblyopes, as in the control subjects, is significantly greater than that of the other retinal positions (table 6).

The amblyopic eye shows a marked depression of critical flicker frequency at the fovea. Table 6 compares the critical flicker frequency values of the amblyopic eye at the fovea with those of the other positions. It will be seen from this table that the foveal critical flicker frequency in the affected eye

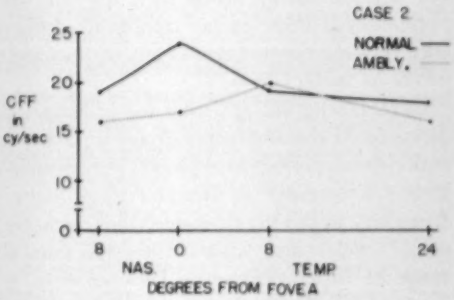


Fig. 2B (Feinberg). Critical flicker frequency curves for Case 2.

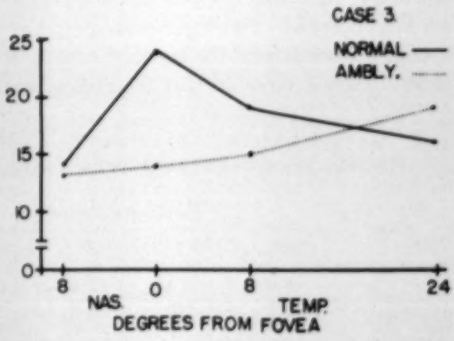


Fig. 2C (Feinberg). Critical flicker frequency curves for Case 3.

TABLE 2

"t" VALUES OF THE MEAN CRITICAL FLICKER FREQUENCY DIFFERENCE BETWEEN EYES OF THE CONTROL GROUP AT EACH RETINAL POSITION

Position	"t"	p Level
24°T	0.26	>0.05
8°T	0.26	>0.05
0°	0.26	>0.05
8°N	0.92	>0.05

TABLE 3

"t" VALUES OF MEAN DIFFERENCE BETWEEN MEAN CRITICAL FLICKER FREQUENCY AT FOVEA AND OTHER POSITIONS IN CONTROL GROUP

Comparison	Mean Difference	"t"
0°–24°T	10.4	13.68****
0°– 8°T	9.1	11.97****
0°– 8°N	9.7	12.76****

**** $p < 0.001$.

does *not* differ significantly from the critical flicker frequency at the other positions. This is in contrast with the previously noted findings for the normal eye, as well as for both eyes of the controls. Further, only the foveal critical flicker frequency of the amblyopic eye is significantly lower than that of the normal eye; there is no significant difference between the two eyes at any of the other positions tested (table 7).

Case 4, who did not meet the criteria for inclusion in the amblyopic group in that she experienced persistent diplopia, also demonstrates a decrease in foveal critical flicker frequency in the involved eye. This decrease of 2.7 cycles/sec., while within the normal range of foveal differences between eyes, is in the same direction as that found in the experimental group.

During the experimental procedure, it was noted that the fixation light tended to fade, when viewed with the amblyopic eye. Cases 1, 2, and 3 reported this phenomenon spontaneously: they described it "as if the light becomes eclipsed," "the light looks as though it comes from around the corner," "the light fades." Case 2 reported that the fading was accentuated when he opened his normal eye, even though the normal eye was covered with a patch and he could not see through it. Case 4 did not spontaneously report any similar experience, and denied it on direct questioning. None of the amblyopic subjects had similar experiences when fixating with their normal eyes, and none of the control subjects reported such phenomena.

Discussion

Nature of the visual disturbance

Our results show that critical flicker frequency is depressed at the fovea of the affected eye in amblyopia ex anopsia. This depression of critical flicker frequency appears in the same area in which acuity is depressed (Duke-Elder, 1949). Critical flicker frequency at other positions tested is not different from that found at the corresponding positions in the normal or control eyes. Since critical flicker frequency is considered a basic feature of light perception, as contrasted with a higher level of visual function, such as pattern vision, one can no longer maintain that impairment in amblyopia ex anopsia is restricted to such higher levels.

The fading of the fixation point when viewed with the amblyopic eye may represent an abnormal fatigue of the visual mechanism. If borne out, this interpretation would be of added interest since an abnormal fatigue has also been noted in visual agnosia (Bay, 1953), which is the other condition cited as representative of selective impairment of higher visual function.

If one postulates that in amblyopia ex

TABLE 4

CRITICAL FLICKER FREQUENCY AT EACH RETINAL POSITION IN EACH EYE OF AMBLYOPIC SUBJECTS

Case	Amblyopic Eye				Normal Eye			
	24°T	8°T	0°	8°N	24°T	8°T	0°	8°N
1	14.9	17.9	17.0	17.4	16.3	19.1	24.0	17.9
2	16.4	19.9	16.9	16.4	17.4	18.9	23.8	18.6
3	19.4	14.7	14.3	14.1	15.5	19.2	23.7	14.7
Mean	16.9	17.5	16.1	16.0	16.4	19.1	23.8	17.1

TABLE 5

CRITICAL FLICKER FREQUENCY IN A SUBJECT WITH CLINICAL DIAGNOSIS OF AMBLYOPIA EX ANOPSIA AND PERSISTENT DIPLOPIA

	24°T	8°T	0°	8°N
Normal	20.4	22.2	27.4	22.1
Involved Eye	21.1	21.4	24.7	23.1
Difference	0.7	0.8	2.7	1.0

anopsia there develops a mechanism characterized by (a) suppression of the image in the deviated eye, preventing diplopia, (b) depression of visual acuity, and (c) disturbance of light perception, it appears that these changes might not occur pari passu. Thus, Case 4 demonstrates intermittent, still troublesome diplopia, fairly marked amblyopia (equal to that in Case 2), but no significant involvement of light perception as measured with our technique. The alterations in the several functions may occur at different rates; further investigation, using a variety of tests, may elucidate the natural history of the disease. Such studies might furnish information of value in determining the optimal time for retraining, and in gauging its success.

RELATION TO EARLIER FINDINGS

Teräskeli and Miles. Our findings are somewhat different from the critical flicker frequency changes reported by Teräskeli (1934) and Miles (1949). We find that critical flicker frequency is depressed in the fovea of the amblyopic eye but is not altered at the other positions tested. Teräskeli measured critical flicker frequency at two positions: foveally and at 10 degrees temporal from the fixation point. In the normal eye, she found critical flicker frequency to be consistently higher in the periphery than in the fovea. In the amblyopic eye this difference was reduced, partly due to an increase in the foveal critical flicker frequency and partly to a decrease in the peripheral critical flicker frequency. Miles does not analyze his data in this manner, but he also finds that the mean difference between the foveal critcal flicker frequency and that at a point eight degrees temporal is reduced in the amblyopic as compared with the normal eye. We cannot account for the difference between these results and those of the present investigation; it probably results from differences in the conditions of stimulation. In any event, the results of the earlier studies agree with our own, insofar as an alteration

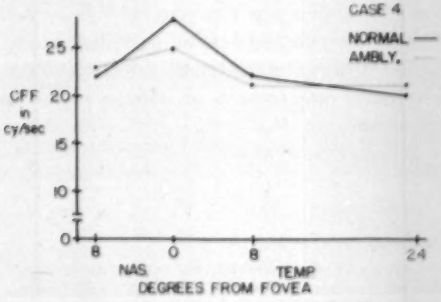


Fig. 3 (Feinberg). Critical flicker frequency curves for Case 4.

TABLE 6

"T" VALUES OF MEAN DIFFERENCE BETWEEN FOVEAL CRITICAL FLICKER FREQUENCY AND THAT OF THE OTHER POSITIONS FOR NORMAL AND AMBLYOPIC EYES

Positions Compared	Normal Eye	Amblyopic Eye
0°–24°T	6.79****	0.73[1]
0°– 8°T	4.31****	1.28[1]
0°– 8°N	6.15****	0.09[1]

**** $p < 0.001$.
[1] $p > 0.05$.

TABLE 7

"T" VALUES OF MEAN DIFFERENCE BETWEEN NORMAL AND AMBLYOPIC EYES OF AMBLYOPIC SUBJECTS AT EACH RETINAL POSITION

Position	Mean Difference Between Eyes	"t" Between Means
24°T	0.5	1.0[1]
8°T	1.6	1.47[1]
0°	7.7	7.06****
8°N	1.1	1.01[1]

**** $p < 0.001$.
[1] $p > 0.05$.

of critical flicker frequency is found in the amblyopic eye by all investigators.

The perimetric fusion thresholds obtained in the normal eye with our technique show a maximal critical flicker frequency at the fovea with decreasing values as distance from the fovea increases. Such a curve, as we have stressed before, has been found consistently by other investigators using the same equipment in this laboratory. Another source of confidence in our present experimental results is the method of ensuring fixation by maintaining a luminous patch in the blindspot.

Wald and Burian. Our findings supplement, rather than contradict, those of Wald and Burian. However, the theory they present—that of a selective impairment of pattern vision with light perception preserved—is called into question by our observations. It is noteworthy that intermittent stimulation revealed a deficit in light perception which tests of absolute threshold, spectral sensitivity, and dark adaptation failed to reveal. The studies of Bender (1947) and Teuber (1950) have repeatedly demonstrated that subtle alterations in perceptual function may be elicited when multiple or recurrent stimulation (permitting stimulus interaction) is employed.

Wald and Burian adduce the results of ablation experiments as giving evolutionary sanction to their separation of visual function. Thus they state that "sub-human mammals, which have been deprived of the occipital lobes of the cerebral cortex, . . . also lose virtually all capacity for pattern vision while retaining sensitivity to light, brightness perception, and visual space localization." However, Klüver (1942) has demonstrated that, in monkeys, the residual light perception involves a response to total luminous flux. This mode of response has never been observed in the intact animal, and is to be distinguished from brightness discrimination as it is usually understood. It therefore cannot be claimed that such phenomena represent a separation of specific visual functions which normally coexist in the intact animal. One further remark may be made in this regard: when pattern vision is lost in occipital-lobectomized animals, it is lost completely—that is, the animals cannot differentiate between a circle and a triangle no matter how large these patterns are drawn. However, in amblyopia ex anopsia, the amblyopic eye can discriminate between such patterns only if they are increased sufficiently in size. Thus the alleged impairment of pattern vision as a higher visual function means something other in the terms of Wald and Burian than in terms of the literature on ablation studies.

Undoubtedly, neither Wald and Burian nor I can give an etiologic account of amblyopia ex anopsia. Neither approach reveals the level in the visual system at which impairment occurs, nor do we know whether "suppression" or "disuse" are meaningful terms to employ in describing the cause of this condition.

Summary

Flicker fusion threshold (CFF) was determined at four retinal positions in three cases of amblyopia ex anopsia. These subjects showed a marked depression of critical flicker frequency in the foveal area of the amblyopic eye. This depression was highly significant when compared with the values obtained in the fovea of their normal eye or the fovea of control subjects.

The finding of a depression in critical flicker frequency which parallels, in retinal distribution, the depression in visual acuity, argues against certain views which postulate a selective impairment of pattern vision in this condition.

Boston City Hospital.

Appendix

A. Amblyopic subjects

Case 1. D. N., a 27-year-old man, a neurologist. Snellen acuity: 20/200, O.D.; 20/20, O.S. Internal squint of the right eye was first noted at age of two years, following a severe right ear infection. Acuity in O.D. was consistently at 20/200 until

age 20 years when two cosmetic operations were performed. Binocular diplopia was severe for the first two weeks postoperative, and there was acuity improvement in the right eye to 20/80 at this time. Diplopia rapidly subsided until it was noticeable only with special attention, and acuity dropped to its present level. The diplopia now elicited under special conditions follows the law of the visual angle. Monocular diplopia was noted by this subject during the course of the experiment.

Case 2. J. S., a 25-year-old man, a medical student. Snellen acuity: 20/30, O.D.; 20/200, O.S.; with correction 20/30 and 20/100. Left eye operated on at the age of four years. Left eye now deviated externally. He has had severe amblyopia in this eye all his life, and wore glasses until one month before testing. He does not notice diplopia in everyday life; monocular diplopia was observed during the experimental procedure.

Case 3. F. F., a 25-year-old woman, a chemist. Snellen acuity: <20/200, O.D.; 20/15, O.S. Strabismus was first noted at eight months of age, when the right eye was seen to deviate externally. This eye was operated on at age four years. At ages five to six years, occlusion of normal eye was attempted, but the subject did not co-operate. Severe amblyopia persisted in this eye. At the age of 18 years, a cosmetic operation was performed. No diplopia developed postoperatively, nor did visual acuity improve. Monocular diplopia was observed during the experimental procedure.

Case 4. D. L., a 22-year-old woman, a nurse. Snellen acuity: 20/20 — 2, O.D.; 20/100, O.S. Left eye was deviated internally until the age of 10 years; then it deviated externally. Occlusion of normal eye was practiced between nine and 10 years of age. No diplopia occurred at this time.

The onset of binocular diplopia was noted at age 15 years, following attempts at refractive correction which had yielded a substantial response. This diplopia continued and necessitated two operations—one in May, 1953, and the latter in August, 1954. Diplopia remains troublesome in everyday life; it appears to follow the law of the visual angle. Monocular diplopia was noted during the experimental procedure.

B. Controls

Subject	Age (Years)	Snellen Acuity: Uncorrected O.D.	Uncorrected O.S.	Corrected O.D.	Corrected O.S.
1. M. W.	24	20/15	20/15	—	—
2. P. Z.	24	20/70 + 1	20/70 + 2	20/30 + 3	20/20
3. J. F.	30	20/50	20/200	20/15 — 3	20/20 — 3
4. D. J.	28	20/50	20/30	20/30	20/20
5. I. G.	24	20/15	20/20	—	—
6. I. U.	28	20/200	20/100	20/30 + 1	20/40

References

Battersby, W. S.: The regional gradient of critical flicker frequency after frontal or occipital injury. J. Exper. Psychol., **42**:59-68, 1951.

Bay, E.: Disturbances of visual perception and their examination. Brain, **76**:515-550, 1953.

Bender, M. B.: Neurology of the optic and oculomotor systems. In Spiegel (ed.): Progress in Neurology and Psychiatry. New York, Grune & Stratton, **2**:131-147, 1947.

Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis: Mosby, v. 4, 1949, pp. 3837-3847.

Klüver, H.: Functional significance of the geniculo-striate system. In Klüver, H. (ed.): Biol. Symposia, **7**:253-299, 1942.

Miles, P. W.: Flicker fusion frequency in amblyopia ex anopsia. Am. J. Ophth., **32**:225-230, 1949.

Teräskeli, H.: Untersuchungen über die Amblyopie ohne Spiegelbefund bei schielenden und nicht schielenden Augen mittelst der Flimmermethode. Acta Soc. Med. Fenn. Ser. B., **19**:1, 1934.

Teuber, H. L.: Neuropsychology. Chap. III (pp. 30-52) in Recent Advances in Psychological Testing: A Critical Summary. Springfield, Ill., Thomas (Amer. Lecture Series, No. 81), 1950.

Teuber, H. L., and Bender, M. B.: Changes in visual perception, apparent motion and real motion after cerebral lesion. Am. Psychologist, **3**:246, 1948.

Wald, G., and Burian, H. M.: The dissociation of form vision and light perception in amblyopia ex anopsia. Am. J. Ophth., **27**:950-963, 1944.

Walsh, F. B.: Clinical Neuro-ophthalmology. Baltimore, Williams & Wilkins, 1947, pp. 268-269.

METIMYD®: A CLINICAL STUDY*

IRA A. ABRAHAMSON, JR., M.D., AND IRA A. ABRAHAMSON, SR., M.D.
Cincinnati, Ohio

Scientific research and clinical analysis of newer ophthalmic drugs is constantly being carried on and evaluated. The value of the topical corticosteroids in the treatment of various ocular diseases is now well established. As described previously in the literature by Lepri,[1] Smadel,[2] Maylath and Leopold,[3] Leopold,[4] Rome,[5] Spain and Molomut,[6] Woods,[7] and Gordon,[8] the simultaneous administration of corticosteroids, sulfonamides, and antibiotics exerts an ameliorating influence on the course of many ocular infections.

Using the combined action of the newer more potent corticosteroid, prednisolone, an effective anti-inflammatory and antiallergic drug, plus the time-tested sodium sulfacetamide, a potent chemotherapeutic agent against Pseudomonas aeruginosa, most gram-negative and gram-positive bacteria, as well as several viruses, an eyedrop was prepared which is now called Metimyd®.

This report covers our observations using topical Metimyd® on over 350 patients with a variety of external ocular afflictions. In most cases the results were very good and usually accompanied by rapid relief of symptoms.

CLINICAL PROPERTIES

Most clinical and experimental studies indicate prednisolone to be two to four times more potent than cortisone or hydrocortisone,[9-11] respectively. The topical application of various concentrations of both its alcohol and acetate forms reveal prednisolone acetate (0.5 percent) the more favorable ophthalmic preparation.[8] Since it has been shown that corticosteroids decrease the reaction of organisms to stress and have definitely effective beneficial antiallergic and anti-inflammatory properties, it was used here as prednisolone in the preparation called Metimyd ophthalmic suspension.

The sulfonamides have shown certain practical advantages, such as notable absence of allergic properties, when applied topically in external eye diseases.[10] Other than producing an occasional mild irritation and a possible bacterial resistance, sodium sulfacetamide has proven to be an effective counter-agent against almost all bacterias as well as intermediate groups of viruses—APC, trachoma, inclusion conjunctivitis, and so forth. It is also highly soluble, stable in solution, and economical. Prednisolone does not interfere with the action of the antibiotic or bactericidal agents, but rather enhances their effect by diminishing the intensity of the inflammation, thus favoring the course of healing. With this in mind, sodium sulfacetamide was combined with prednisolone acetate and neomycin sulfate to produce Metimyd ophthalmic ointment.

CLINICAL STUDIES

The clinical study of Metimyd ophthalmic suspension and ointment was in most cases limited to the local application of these preparations to a large series of cases showing various external ocular diseases. Even though Meticorten and Meticortelone were given systemically to several of these patients, it is not the scope of this paper to discuss the systemic effect of these drugs which has been amply covered by King and Weimer,[11] Gordon,[8] Leopold,[4] Hogan,[12-13] and others.

The aqueous suspension was used as eyedrops instilled every hour until the condition improved, at which time the drop interval was increased. The ointment, when used, was used one to three times daily, but when

* From the Department of Ophthalmology, University of Cincinnati School of Medicine, and the Jewish and General Hospitals. Prednisolone plus sodium sulfacetamide (Metimyd) used in this study was supplied by Harry V. Pifer, M.D., Clinical Research Division, Schering Corporation, Bloomfield, New Jersey.

combined with the drops was used at bedtime only. Over 350 patients were treated with either or both preparations and no ill effects other than a slight burning sensation, lasting seconds, were encountered.

The results, using these preparations, were quite dramatic in the majority of cases treated. The authors had previously used a preparation of Cortomyd* ophthalmic ointment and suspension for over a year on a very large series of patients with excellent, unpublished results. A comparison between the Metimyd and Cortomyd products reveals very little difference in results—both being equally effective, although the Metimyd was somewhat more rapid in action. Where one failed to clear the condition, the other also failed to produce improvement. This was noticeably seen in dendritic keratitis and certain gram-negative and viral keratoconjunctivitides which respond better to other agents. Two cases of severe iritis failed to respond to the local use of Cortomyd or Metimyd alone but improved when combined with systemic therapy.

The drug was used on the following anterior segment diseases:

Dermatitis

Five patients with an allergic dermatitis of the forehead or cheek, and seven with blepharodermatitis (two of these proved to be staphylococcal in origin), improved remarkably in 24 hours and cleared almost completely in 48 hours after administration of Metimyd ointment three times a day.

Blepharitis

Forty-eight cases of blepharitis, probably due to allergy to the staphylococcus organisms, responsed dramatically to both the drop and ointment form of therapy. Seventeen of these patients had, in addition, acute meibomianitis which partially subsided with less edema and lid reaction under treatment, and later required surgical incision and drainage. Two cleared without surgery. Nine patients with chronic blepharoconjunctivitis improved under local therapy, but required additional systemic staphylococcal toxoid desensitization to prevent recurrence.

Conjunctivitis

A. *Allergic conjunctivitis.* Twelve cases cleared almost completely in 48 hours after topical drop therapy. Two patients with atropine sensitivity were cured in three days after cessation of the atropine and topical use of Metimyd.

B. *Acute, infectious, gram-positive conjunctivitis.* Of 42 patients, 38 made dramatic improvement. The lid edema lessened, the conjunctiva became clear, and the condition subsided within four to seven days after therapy. Four required additional antibiotic treatment.

C. *Acute, infectious conjunctivitis due to gram-negative organisms and viruses.* Except for two cases, due to the Koch-Weeks bacillus, 12 patients responded poorly to this form of topical therapy and required the use of antibiotics to bring about improvements.

Episcleritis

Three patients with nonspecific episcleritis responded successfully to topical Metimyd drop therapy. The pain subsided and the injection disappeared within five to seven days.

Keratitis

Marginal ulcers responded most dramatically to Metimyd therapy, as found by King,[11] and Hogan,[12] with the use of steroids. In six patients the condition had completely cleared in 24 hours. These were probably of staphylococcal origin or due to sensitivity from staphylococcal lid infection. Following the removal of foreign bodies in 18 patients, the instillation of Metimyd suspension or ointment met with no untoward effect in 16. Two patients developed dendritic keratitis which responded satisfactorily to iodine cautery and antibiotics.

* Supplied by Schering Corporation, contains Cortisone.

As shown by other authors (King,[11] Hogan,[12,13] Gordon[6]), the use of steroids tends to make most cases of acute dendritic keratitis worse and are therefore contraindicated when this condition is present.

Three patients with epidemic keratoconjunctivitis, and four with superficial punctate keratitis, showed only slight improvement with lessened edema under Metimyd therapy, but required antibiotics for additional improvement. Acute central corneal ulcers responded poorly in two cases where Metimyd drops were used topically, alone, for four days. Specific antibiotic therapy produced satisfactory improvements.

Iritis

Nine patients with nongranulomatous iritis, and five with granulomatous iritis, were treated with local application of Metimyd drops accompanied by neosynephrine (10 percent) and Antrenyl[14] (5.0 percent). All but two of the granulomatous types made satisfactory improvements within seven to 12 days with this form of therapy. These two cases required additional combined systemic therapy of antibiotics and Meticortelone. It should be noted that a routine survey was performed on all 14 patients and only three showed possible foci, for which treatment was instituted.

Postoperative cases

A total of 92 major surgical cases, for example, cataracts, glaucoma, strabismus, enucleations, and so forth, were given topical Metimyd in drop and/or ointment form, postoperatively, without producing any untoward reaction. Lid and conjunctival edema was lessened, but subconjunctival hemorrhage or hyphema tended to persist longer under Metimyd instillation.

Thirty-nine minor surgical cases—postoperative chalazions, pterygiums, and so forth—received Metimyd routinely with results similar to those previously stated.

Conclusion

Meticortelone has been shown to be more effective than any of its steroid predecessors, possessing strong anti-inflammatory and antiallergic properties. The combination of this drug with sodium sulfacetamide (10 percent), a potent bactericidal agent, has produced a valuable adjunct in our ophthalmic armamentarium. Metimyd is indicated in ocular allergies, edema, and inflammation producing dermatitis, blepharitis, conjunctivitis, episcleritis, marginal ulcers, or iritis. It is contraindicated in acute dendritic keratitis, acute central corneal ulcers, subconjunctival hemorrhage, hyphema, and principally in herpes simplex ophthalmicus. A combination of topical and systemic therapy is recommended for severe cases of iritis.

Summary

Metimyd, the combination of a new potent steroid, prednisolone acetate, and the time-tested chemotherapeutic agent, sodium sulfacetamide, with the antibiotic, neomycin sulfate, has been used successfully with few untoward effects on over 350 cases exhibiting various ocular and anterior segment diseases. There has been no harmful influence from a combination of these three agents except as indicated.

925 Fifth-Third Bank Building (2).

References

1. Lepri, G.: Studies on cortisone in ophthalmology, Am. J. Ophth., **35**:935-946 (July) 1952.
2. Smadel, J. E.: Treatment of typhoid fever. Ann. Int. Med., **34**:1-9 (Jan.) 1951.
3. Maylath, F., and Leopold, I. H.: Study of experimental intraocular infection. Am. J. Ophth., **40**: 86-101, 1955.
4. Leopold, I. H., et al.: Cortisone in ocular disease. Am. J. Ophth., **34**:361-371, 1951.
5. Rome, S., et al.: ACTH and cortisone in ocular inflammations: Parental and local use. Ann. West. Med. & Surg., **4**:799-804, 1950.
6. Spain, D. M., and Molomut, N.: Effects of cortisone on development of tuberculosis lesions in guinea pigs and on their modification by streptomycin therapy. Am. Rev. Tuberc., **62**:337-344, 1950.

7. Woods, A. C.: Clinical and experimental observation on use of ACTH and cortisone on experimental ocular inflammatory diseases. Am. J. Ophth., **33**:1325-1348, 1950.
8. Gordon, D. M.: Prednisone and prednisolone in ophthalmology. Am. J. Ophth., **41**:593 (Apr.) 1956.
9. Leopold, I. H., Kroman, H. S., and Green, H.: Intraocular penetration of prednisone and prednisolone. In press.
10. Theodore, F. H.: The use of sulfirgamide in external diseases of the eyes. Am. J. Ophth., **40**:406-411 (Sept.) 1955.
11. King, J. H., and Weimer, J. R.: Prednisone (Meticorten) and prednisolone (Meticortelone) in ophthalmology. Arch. Ophth., **54**:46-54 (July) 1955.
12. Hogan, M. J., Thygeson, P., and Kimura, S.: Uses and abuses of adrenal steroids and corticotropin. Arch. Ophth., **53**:165-176 (Feb.) 1955.
13. ———: Effects of prednisone and prednisolone in ocular inflammation. In press.
14. Abrahamson, I. A., Jr., and Hurwitz, P.: Antrenyl: A substitute for atropine. Arch. Ophth., **52**:519-524 (Oct.) 1954.

Ophthalmic Miniature

Treatment of the eyes after illness

His anguish was much augmented by a tenderness of the brain which tended not a little to increase the weakness of the eyes, so much so, indeed, that when I was called in I found my patient in the most deplorable state. His friends had placed him in a darkened apartment, where they had most injudiciously quacked him with various boasted remedies; all these immediately changed, and my first object was to prescribe for him a solid and nourishing diet, accompanied by cheerful company at his meals, then a glass of good wine, moderate exercise in the open aire, and, finally, the use of a clear and equal light. He continued this simple regimen for some time; and, in the agreeable society of his family and friends, soon forgot his disorder, which totally disappeared, in fact, at the end of three weeks, although he had been taught to fear the approach of a gutta serena, and his eyes were soon as good as before his illness, and equally able to support a continued degree of tension.

H. Colburn, London, 1816.

NOTES, CASES, INSTRUMENTS

A LIGHTING SYSTEM FOR A TWO-METER TANGENT SCREEN*

MYLES M. BERK, M.D.
Pittsburgh, Pennsylvania

In order to facilitate greater accuracy in my central field examinations I have devised a new fluorescent lighting system for a two-meter tangent screen. This system gives an even light intensity over the entire field and the light intensity can be varied without varying the quality of the light.

The system consists of two F96T12 Slim-Line fluorescent bulbs surrounded by two aluminum tubes mounted on eight-foot standard white fluorescent channel fixtures. The fixture is fastened to a plywood base by three metal straps, and stood vertically. The outer aluminum tube is attached to the fluorescent fixture and has one one-half inch linear aperture. The inner tube has four one-half inch linear apertures. It is suspended within the outer tube so as to be easily rotated through 360 degrees.

Three slots of the inner tube are covered by gelatin theatrical filters of red, green, and blue; the fourth is left without a filter. Thus the color can be changed by rotating the inner tube.

The light intensity can be changed by the amount of aperture in the inner tube which is left exposed through the opening in the outer tube or by moving the lighting system closer or farther from the screen. With full aperture and white light it was found that 10 foot-candles fell on the screen if the lights were placed at one meter's distance. There is very little variation of light intensity over the entire area of the screen (fig. 1).

With this system, only white test objects are necessary as the color of the object is changed by rotation of the inner tube. This has the advantage of being able to measure easily the intensity of the light, including that of the colored light. The filters may be checked on a spectrophotometer to get their transmission wavelengths.

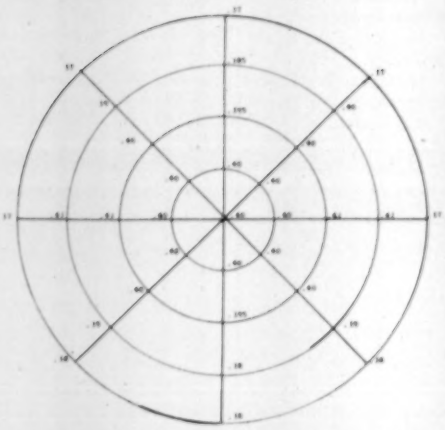


Fig. 1 (Berk). Variation of light intensity over the two-meter tangent screen, as measured with a photomultiplier so that a reading of 0.40 ma. equals approximately 10 foot-candles on a standard General Electric exposure meter.

Without filters this system produces 10 foot-candles of white light; with the colored filters in place the amount of light intensity is therefore low. This is partially overcome if one remembers that when he does a field with a colored test object he does not increase the intensity of his white light to compensate for the fact that these objects reflect only a percent of the total light projected on them. With the filters the intensity of the transmitted colored light can be measured easily. It is, however, difficult to measure the amount of light reflected from a small colored test object.

Placement of the lights is important and must be determined with the help of a light meter so as to give even light over the screen. As the lights are moved closer to the screen there is a greater variation in

* From the Department of Ophthalmology, University of Pittsburgh School of Medicine, and the Eye and Ear Hospital.

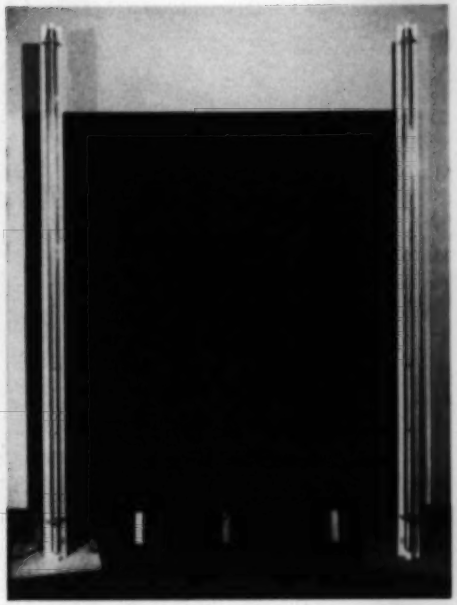


Fig. 2 (Berk). View of light and tangent screen before wall was painted black.

light intensity over the screen. Once in place, if the floor is marked, there need be no further checking of light except periodically to note the changes in the fluorescent bulbs. A fluorescent bulb loses 10 percent of its efficiency in its first 100 hours of use and then about 20 percent in the rest of its rated life (7,500 hours for a T12 Slim-Line), so that after 100 hours the light is relatively constant.* To prevent reflection, the wall surrounding the screen should be painted dull black or covered with black felt. Once the floor is properly marked the lighting unit can be moved against the screen for storage, taking up little office space. For details of construction see Figure 2.

Summary

A lighting system for a two-meter tangent screen as described gives even light over the entire screen. With this system the light intensity can be varied without changing the quality of the light. The lighting system requires only white test objects. These factors make this an efficient office lighting system.

Eye and Ear Hospital (13).

* General Electric Booklet LS-102, "Fluorescent lamps," p. 11.

CARRIER FOR CATARACT-MASK STRING

Peter Chao, M.D.
Mineola, New York

After intraocular surgery, most eye surgeons have felt the need of some method of passing the strings of a cataract mask around the patients neck without having the patient lift his head off the operating table.

In order to pass the strings of the mask behind the patient's head, a wire coat hanger was stretched out by grasping it at the middle and pulling it into a long narrow loop. The hook was bent to form a ring.

The patient is instructed not to help when the carrier is passed under his neck, if he is lightly sedated. The carrier is passed under the neck. The strings on the left side will be carried to the right; those on the right to the left (fig. 1.) The strings are then tied at the forehead.

This simple device has been found to be effective and is used routinely after intraocular operations for pulling the strings of a cataract mask around the patient's head without movement of the patient's head.

Nassau Hospital.

Fig. 1 (Chao). Passing the cataract-mask strings under the patient's head.

A POCKET FLASHLIGHT WITH INTERCHANGEABLE TIPS*

Designed especially for eye examinations

Conrad Berens, M.D.,
George Z. Carter, M.D.,
and
Arnold S. Breakey, M.D.
New York

Since the introduction of the original pocket flashlight in 1954,[1] several improvements and additional attachments have been made.

A change in the original size of the flashlight was found to be desirable because of the difficulty in obtaining the small batteries. The new flashlight (fig. 1), is 16 cm. in length, the barrel is 12 mm. in diameter, thus accommodating larger sized batteries which are readily available. The new barrel will also accommodate the long-lived mercury batteries.† The general construction is identical to that of the previously reported flashlight except that it is made of light weight aluminum rather than brass.

The need for a device for studying retinal response in cataract patients, motivated the development of an additional interchangeable tip (fig. 1-A).

The new attachment contains four openings with a diagonal distance of six mm. between the openings which are spaced five mm. apart. The openings project four lights, two white which are each one mm. in diameter and one red and one green, each 0.5 mm. in diameter. By rotating the diaphragm, one to three lights may be exposed in the following combinations: two white; one white, one red, one green; one green; one red, one green; two white, one red; and one white.

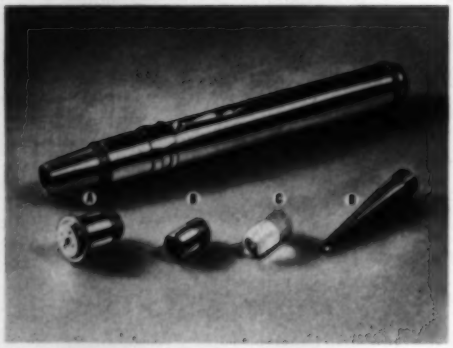


Fig. 1 (Berens, Carter, and Breakey). A sterilizable flashlight without springs or switch. Interchangeable tips include: (A) Multiple spot head. (B) Cobalt blue tip. (C) Plastic focal illuminator. (D) Right-angled plastic transilluminator.

In testing central vision in patients with advanced cataract, the light is held 10 cm. from the eye and the colors and white lights projected on the patient's pupil. Patients with uncomplicated mature cataract can name the red and green lights and can see all the combinations of red, green, and white lights as well as the two white lights when the batteries are discharging one volt. The ability to perceive red and green lights is also of value in detecting possible disease of the optic nerve and for detecting scotomas in patients with macular disease and paracentral field defects.

In studying motor anomalies, the one-mm. white light may be used for fixation and for using the Maddox rod and prisms at near. By turning the diaphragm and by showing lights of different colors, attention and fixation can be stimulated in young patients when performing the screen and parallax test, Maddox rod, and excursion tests.

The lights which form a triangle exposing the white, red, and green may be used as a three-dot test for near if the red and green spectacles used in the three-character test[2] for binocular vision are worn.* If binocular

* From the Department of Research, New York Association for the Blind, and the Department of Ophthalmology, New York University Postgraduate School of Medicine. Aided by a grant from The Ophthalmological Foundation, Inc. Made by R. O. Gulden, Philadelphia 20, Pennsylvania.

† P. R. Mallory & Co., North Tarrytown, New York.

* Made by R. O. Gulden, Philadelphia 20, Pennsylvania.

vision is present, one white-tinged red or green, one red, and one green dot are seen. If diplopia exists, two red and two green dots will be seen and, if either eye is suppressing, either two red or two green dots will be seen.

The second interchangeable tip contains a cobalt glass (fig. 1-B) which enables one to see more readily fluorescein-stained areas of the cornea. It is most efficacious when used in a darkened room.

The rounded plastic tip (fig. 1-C) forming a dot beam for focal illumination, and the right-angled transilluminator tip (fig. 1-D) have been described previously.[2]

The plastic illuminated retractor,[3] which is useful in surgery of the oblique muscles and in operations for retinal separation, also fits this flashlight.

As previously stated,[1] the pocket flashlight contains no springs or switch which might wear out. The three metal parts of the flashlight may be boiled or sterilized in alcohol and the bulb and batteries are then replaced. Neither alcohol nor boiling water should be used for sterilization of the plastic tips. These attachments may be sterilized in C.R.I. Germicide (methyldodecylbenzyltrimethyl ammonium chloride 17.5 percent and inert ingredients by weight, 82.5 percent) in 1:100 dilution, or aqueous benzalkonium chloride (Zephiran) 1:1,000 dilution.

The flashlight with its various attachments has been found to be valuable for clinic, office, hospital, and emergency examinations.

708 Park Avenue (21).

REFERENCES

1. Berens, C.: Pocket flashlight for physicians with focal illuminator and transilluminator. J.A.M.A., **155**:124 (May) 1954.
2. ———: A modified 3-character test for binocular vision. Arch. Ophth., **41**:460 (Apr.) 1949.
3. ———: Transilluminators and illuminated retractors for retinal detachment, muscle and tumor surgery. J.A.M.A. In press.

METAHERPETIC KERATITIS

NOTES ON TREATMENT

ALGERNON B. REESE, M.D.
New York

If the infection of herpes simplex involving the corneal epithelium is not arrested in the early stages by the usual treatment of curretage of the infected epithelium, followed by the application of iodine or some drug to the denuded area, a protracted course may ensue lasting for several months. This metaherpetic stage of the disease demonstrates few if any of the characteristics of dendritic keratitis. Instead, we are likely to observe a more or less diffuse involvement of the central portion of the cornea which is not unlike keratitis neuroparalytica. A decrease in the corneal sensitivity may be marked. As herpes simplex is a neurotropic virus it seems probable that neurotrophic changes are an important feature in the metaherpetic stage. I have, therefore, employed lid adhesions in this stage with good results.

When the lid margins are denuded of their epithelium in order to produce lid adhesions, I prefer to leave unclosed a central area of approximately eight mm. This small opening in the lids permits the observation of the cornea. The adhesions are allowed to remain for approximately two months or less. Healing of the corneal lesion with epithelization and return of luster progresses after the lids have been closed.

73 East 71st Street (21).

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

SWISS OPHTHALMOLOGICAL SOCIETY

Lausanne, September 30 to October 2, 1955

STRABISMUS

A symposium on strabismus was introduced by DR. R. HUGONNIER (Lyon) and DR. BANGERTER (St. Gall) who discoursed in turn on the general principles guiding diagnosis and treatment. DR. A. HUBER AND DR. F. H. LEHNER (Zurich) surveyed their experience with electromyography and recommended its clinical use. The question of a partial or total paresis of an ocular muscle can thus be decided. DR. F. RINTELEN (Basle) discussed his surgical results with complete tenotomy and concluded that recession is a safer procedure. Nevertheless, he advised partial tenotomy for a convergent strabismus of less than 12 degrees. DR. E. B. STREIFF and DR. A. RICCI (Lausanne) considered early surgery—between ages three to five years—as most desirable. DR. F. KÖNIG AND DR. E. LANDOLT found that 80 percent of their cases of divergent strabismus followed operative overcorrection of convergent strabismus. They intervened regularly on the tenotomized muscle. DR. J. LANG (Zurich) treated eccentric fixation by Cüppers method of direct macular stimulation, using a light strong enough to produce a macular after-image. Orthoptics was discussed respectively by DR. H. SMOLIK (Montreux) and by DR. A. AND DR. M. RICCI (Lausanne).

GLAUCOMA

DR. H. GOLDMANN AND DR. T. SCHMIDT (Basle) have installed a testing station for Schiøtz tonometers and from their examinations would suggest certain modifications in construction. DR. F. GAFNER (Liestal) emphasized the value of angioscotometry for early diagnosis. DR. J. F. CUENDET (Lausanne) found that attacks of acute glaucoma are particularly frequent at new moon and full moon. DR. F. FANKHAUSER AND DR. T. SCHMIDT (Basle) recommended the fistulizing operation of Preziosi which is accomplished by a special cautery. DR. F. MARTY (Geneva) reported three cases of glaucoma and one of pseudoglaucoma associated with suprasellar tumor. Campimetry showed atypical fields in two cases.

RETINAL DETACHMENT

DR. M. AMSLER (Zurich) paid tribute to Gonin on the 20th anniversary of his death and pointed out that the modifications of his operation but serve to apply more effectively the fundamental principles that he enunciated. DR. G. MAEDER (Geneva) utilized the Schepens technique in 20 complicated cases with successful results in 15. DR. H. R. BÖHRINGER (Zurich) found that the incidence of detachment paralleled the degree of myopia, his cases in high myopia (over 10D.) numbering 45; in moderate myopia (5.0D. to 9.0D.) 25; and in mild myopia (2.0D. to 4.0D.) seven.

CORNEA

DR. J. BABEL (Geneva) reported five cases of edematous keratitis lasting several months which seemed to be due to a virus related to that causing epidemic keratoconjunctivitis. DR. STEIGER (Berne) described a case of filiform keratitis associated with fatal encephalitis.

CLINICAL OBSERVATIONS

DR. FAVRE (Berne) discussed syphilitic optic perineuritis which shows typically a papillitis without disturbance of visual function. With prompt antiluetic treatment the prognosis is good.

Dr. F. Verrey (Zurich) reported that a new drug related to chlorpromazine administered to 84 patients provoked a pigmentary degeneration of the retina in 11 and milder subjective or objective findings in 13. The acuity, visual field, and adaptation were affected.

Dr. E. Rosselet and Dr. P. Magnenat (Lausanne) mentioned a case of tuberculous uveitis associated with purpura in which the Mantoux test was negative while puncture biopsy of the liver was positive. The latter test is of diagnostic value as it is negative in rheumatoid and sarcoid lesions.

Dr. Rintelen and Dr. G. Saubermann (Basle) in the Ridley operation find that meticulous irrigation of the sterilized lenticulus with isotonic saline for 30 minutes diminishes postoperative iritis. An eye in which a successful operation had been performed 18 months previously was obtained from a patient, aged 70 years, who happened to die of cancer. Histologic study showed that organized exudate was limited to the posterior surface of the iris and the adjacent pupillary area. The hyaloid membrane was unaffected. Postoperative fibroplasia resulted in a tenuous circular adhesion of the iris root to the corneoscleral trabecula. Examinations before death, however, had revealed no ocular irritation nor secondary glaucoma.

Experimental investigation

Dr. R. Bruckner, Dr. E. Sutter, Dr. R. Schenkel, and Dr. G. Huber (Basle) presented histologic slides of the central retinal area of various mammals and discussed the significance of comparative biology.

Dr. R. Sampaolesi (Zurich) studied the blood-vitreous barrier in aphakia by the fluorescein test of Amsler and Huber in 35 cases and demonstrated the diffusion of fluorescein into the vitreous.

John D. Blum (Geneva),
Correspondent.
James E. Lebensohn,
Translator.

YALE UNIVERSITY CLINICAL CONFERENCE

May 13, 1955

Dr. R. M. Fasanella, *presiding*

Ophthalmic plastic surgery

Dr. Sidney A. Fox (New York) gave a talk on many of the more common problems in ophthalmic plastic surgery and illustrated the points mentioned by numerous beautiful color photographs. He introduced the subject by reiterating the six fundamentals of ophthalmic plastic surgery:

1. Incisions should be made parallel to the lid margins, if possible.
2. Lid splitting.
3. Lid halving.
4. Tarsorrhaphy.
5. Canthotomy and cantholysis.
6. Replacing lid tissue with lid tissue.

In regard to the first principle, that of making incisions parallel to the lid margin, Dr. Fox noted that one cannot always observe this principle. It is a good general rule, however, because most of the wrinkles are parallel to the lid margin. Likewise, such an incision would be parallel to the orbicularis fibers. Rarely does one have to worry about blood supply in the lids.

Lid splitting is easily done between the tarsus conjunctiva layer and the muscle skin layer.

Lid halving affords a greater healing surface and lessens the tendency to scarring.

Tarsorrhaphy is important in protecting the cornea. It also splints the lids. Dr. Fox leaves his sutures in for 10 days unless the suture is loose. He also described a technique using a sliding tongue of tarsus for a firmer tarsorrhaphy.

A simple canthotomy always heals well without sutures. If more room is needed, one should cut the corresponding branch of the external canthal ligament, either the upper or the lower branch. This procedure will release additional space for lid motion.

The subject of chalazions was next dis-

cussed. Dr. Fox defined a chalazion as a chronic granuloma of the tarsal glands. He noted there were three general methods of handling a chalazion: (1) Cut and squeeze methods; (2) cut and cauterize; (3) cut and excise.

Three modes of attack were also possible: the external, the internal, or the marginal, and his feeling was that the mode of attack depended on where the chalazion points. By the external route, a horizontal incision was made externally. The anterior surface of the chalazion was excised, the contents were scooped out, the interior was cauterized with iodine, and the wound sewed with several sutures. By the internal method, a vertical incision was made. The posterior surface of the chalazion was excised and the contents cauterized with iodine. No sutures are used. To treat a marginal chalazion, cut it off flush with the lid margin, split the tarsus, curette, and cauterize the contents. No sutures are used.

Dr. Fox defined an internal hordeolum as an acute infection in the same place as a chalazion. This is treated in the same way as a chalazion with either an external or an internal approach. The cyst of Moll was next mentioned briefly. It can be treated simply either by excision or desiccation, either method being satisfactory.

Basal-cell carcinoma is a very common and important lesion. Dr. Fox definitely indicated his preference for surgery as against X-ray therapy. For one thing, a specimen was secured in surgery. It is also easier, in his view, to excise the lesion completely and to preserve the cilia and lid margins through surgery, whereas, following X-ray treatment, frequently a goodly number of cilia are lost. X-ray therapy can also cause keratinization of the conjunctiva and some corneal excoriation. Furthermore, if surgery has to be resorted to after X-ray therapy, it must be widespread and is difficult. When a large lesion not involving the lid margin is present, a graft is usually necessary. One should do a tarsorrhaphy then excise the lesion. If possible, one can take lid skin for the graft from the same upper lid. One doesn't need an excess of skin. A firm pressure dressing is important. Dr. Fox doesn't change the dressing for six days. He emphasized the point that it is not necessary to take out lid sutures too early to avoid scar formation. He mentioned that if one takes out sutures too early and the wound is thereby allowed to gape, that would always leave a scar.

The next subject was that of lesions involving the lid margin. Warty growths involving the lid margins are best treated with desiccation. A lesion such as the basal-cell carcinoma has to be excised. Dr. Fox illustrated the important steps in several methods of approach. One approach was that of a triangular type excision combined with the halving method of resuturing. A more extensive lesion requires a rectangular excision creating two sliding flaps. Considerable undermining is necessary until adequate relaxation is achieved. Here again, a halving procedure may be added to the method of resuturing the skin. When the entire lid margin is involved, a more extensive procedure is naturally necessary.

Discussion. Dr. Fasanella: Would you say something about the treatment of spastic entropion and treatment of recurrences.

Dr. Fox: There is no procedure used for spastic entropion without some recurrence. My own procedure has been modified lately so that I am now taking out a triangular tarsal section which is six to seven mm. wide at the base. We have had no recurrences for the past two years.

Dr. Kaplan: What do you do with the skin?

Dr. Fox: I cut out a corresponding section of skin and muscle too. I never worry about the slight ectropion. The lid always reinverts in two or three weeks.

Dr. Glass: It not infrequently happens that one may have to treat a case with four or five chalazions on one lid. Do you modify your procedure in any way in this type of case?

DR. FOX: No modification whatsoever. You do not have to worry about any excessive loss of tarsus.

DR. KOGUT: If you notice that a skin graft is black on the sixth postoperative day, what would you do at that time?

DR. FOX: I would ordinarily debride it and wait until it heals before doing anything else. Usually in this case, there is some factor that interferred with healing rather than poor technique. Ordinarily, I might dress a case with a graft on the fourth or fifth day, put on a firm adhesive pressure dressing, changing it about every three days. The light cover is used after the 10th day.

DR. ROSENTHAL: How thick a lid graft do you use?

DR. FOX: Just skin, very thin.

William I. Glass,
Recording Secretary.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

March 16, 1955

DR. FRANK W. DIMMITT, *presiding*

CATAREX LENS

DR. DEWEY KATZ of Hartford, Connecticut, described his experiences with "The Catarex lens: Its uses and benefits to patients." The Catarex service of the Vision-Ease Corp., St. Cloud, Minnesota, provides postoperative cataract patients with a temporary pair of glasses during the period of convalescence. The service uses round lenses in which the spherical power is ground on the front of a flat base-curve lens that has a reading "add" of the desired power. Cemented to the back of this is the cylindric correction. The lens is mounted in a pair of temporary frames which can be adjusted to the patient's needs. When the refraction finally stabilizes, the patient's final correction is in the temporary glass, and the ophthalmologist can make his final refinement over the "cataract" glass at the vertex distance, position, and so forth, where the patient will ultimately wear the glasses.

The service was explained in detail, and it was pointed out that while many opticians perform this service at no extra charge to the patient, some do charge a nominal fee. After a brief discussion as to whether the assistance was really sufficient to make it worth the effort, Dr. Katz closed by explaining that, in his practice, it was used primarily for those patients whose gainful employment made necessary the use of some temporary device as soon as possible.

SIMPLIFIED PTOSIS SURGERY

DR. BRENDAN D. LEAHEY, Lowell, Massachusetts, presented a movie on "Resection of the levator by the external route." This was a demonstration of the method he described in a paper, "Simplified ptosis surgery," published in the *Archives of Ophthalmology* (**50**:588-596 [Nov.] 1953).

In the discussion which followed Dr. Leahey's paper, it was pointed out that an external approach was much more satisfactory than a conjunctival one because the exposure is much better, that resection of the levator is a much more satisfactory procedure than tucking, and that, in case reoperation is necessary, the field is much cleaner. It was pointed out that the main advantage of the stay suture, which Dr. Leahey described, is to hold the lid up until the muscle is no longer paralyzed. This gives a much greater result from the same amount of muscle resection.

INTERMITTENT ESOTROPIA

DR. FRANK D. COSTENBADER, Washington, D.C., "Diagnosis and management of intermittent esotropia." After presenting a general background of the problem of esotropia, the physiology of strabismus, various diagnostic methods, and an explanation of why he used the term intermittent esotropia rather than accommodative esotropia, he divided the intermittent esotropias into two groups, the incomitant and the comitant.

He outlined certain background causes for cross-eye, including orbital deformities of any considerable degree and their variation, difficulties or lesions in the cortex or subcortex affecting the vergences, versions, and so forth, and some of the general regulatory mechanisms, pointing out that most lesions which affect the nuclei or peripheral nerves are more likely to cause involvement of a single muscle or a single eye. In addition he emphasized innervational and tonic factors in the background of convergent strabismus. He cited the fact that there is some evidence indicating the existence of an active divergence mechanism, and that this is presumably in balance with a tonic convergence mechanism, and that occasionally, as a result of disease, or as a result of the innate disposition of the individual, this mechanism may not be good enough and the eyes will go out of line.

Dr. Costenbader laid particular stress on the accommodative group of convergent strabismus, emphasizing that the convergence is not in proportion to the amount of accommodation, but in proportion to the amount of effort to accommodate. He divided the accommodative cases into two groups; one, with a normal accommodation convergence ratio in which the amount of refractive error alone is responsible for the tendency to converge; and the other, with an abnormal accommodation convergence ratio where there is likely to be a very small refractive error, but the convergence is out of proportion to the accommodation which seems to be exerted. This is attributed either to (a) a basically weak accommodation, or (b) a low threshold of stimulation for accommodation, so that very little accommodative effort would give an exaggerated convergence response.

Counteracting these mechanisms is a divergence tonic mechanism and fusional vergences, although Dr. Costenbader frankly admitted that these latter two factors are somewhat difficult to evaluate at present. Insofar as the fusional vergences are concerned, he made two points clear—if the visual acuity is poor in one eye, the patient is not going to try to fuse very well, or if there is a high degree of aniseikonia or anisometropia, the patient will likewise not be encouraged to fuse. In discussing this problem, he also recognized the fact that there may be some individuals who, under most conditions, just don't want to fuse.

Dr. Costenbader outlined a general pattern of diagnosis: First, determine whether the squint is comitant or incomitant. Second, determine what is the accommodative element as compared to the nonaccommodative. The nonaccommodative element requires surgery; the accommodative element may often be corrected by functional treatment. Third, separate the accommodative group into those with normal accommodation convergence ratio and those with abnormal accommodation convergence ratio, treating the former with single lenses and the latter with bifocals.

He then described in some detail what he considers to be the minimal hyperopic correction needed to handle the accommodative element. This is gradually reduced, if possible, to give the patient single binocular vision without glasses, although it is recognized that it is extremely unusual to be able to get the glasses off of a patient who has more than four diopters of hyperopia.

Dr. Costenbader concluded his background presentation by presenting his own classification of convergent deviations, listing them as latent, intermittent, or constant, having first broken them down into the comitant and the incomitant. Under the intermittent group he listed divergence insufficiency, convergence excess (usually called accommodative).

For the rest of the evening, he discussed the convergent excess group which he divided into three categories: (1) the refractional or those with a high hyperopic refractive error and essentially normal accommodation convergence ratio; (2) poor accommodative power or an abnormal convergence ratio with excessive stimulus to con-

vergence during the exercise of any accommodation whatever, and (3) the "hyper-reactor"—an individual with exaggerated responses for any type of stimulation. Case histories were presented to illustrate these types of cases, and Dr. Costenbader's method of approach to treatment in each different type was described.

In the first group in which Dr. Costenbader feels the squint is entirely due to the degree of hyperopia, the onset is usually not before the age of two years, and usually occurs before the age of five years. The amount of esotropia is usually the same for distance and near, ranging between 10 and 40 prism diopters and is reduced to a phoria when the correction is on. The hyperopic range is generally from two to six diopters, occasionally over seven, but usually whenever the hyperopia is over six diopters, the patient just accepts his blurred vision and does not develop strabismus. A few cases have been seen with a lesser amount of hyperopia, but this is also unusual.

There is usually very little amblyopia and, when present, it responds fairly well to treatment. The retinal correspondence is usually normal. There is a variable degree of fusional vergences.

Treatment is by use of the optimal hyperopic correction. Bifocals are usually not necessary, and the correction is gradually reduced if it is less than three or four diopters. However, if the patient is uncomfortable or tends to turn his eyes in when the correction is reduced, Dr. Costenbader uses whatever strength is necessary to keep the eyes straight and keep the patient comfortable. He has tried miotics on this group, but they have been of questionable help. Orthoptics has been used to help build up fusional vergences and has seemed to be helpful.

There were two qualifying comments on this group: (1) The chances of getting away from glasses are very small if the hyperopia is more than four diopters; (2) if there is any considerable anisometropia, it is very hard to build up fusional vergences and, again, it is rare that glasses can be discarded.

The second group, those with an abnormal accommodation-convergence ratio, usually have a gradual onset, they continue to have esophoria or an intermittent esotropia for distance but show a large esotropia for near, and usually have an insignificant degree of hyperopia (rarely over +1.5D.). The accommodation is remote for the patient's age, binocular visual mechanism may be good but fusional divergence is poor. The theoretic physiology is that the patient has to use much more accommodation than average and therefore gets an additional convergence stimulation. Miotics have proved very helpful in treating this group and bifocals have also been used a great deal.

At this point Dr. Costenbader digressed to point out that no one ever cures squint but helps Nature do it; that the only way really to help, is to keep the vision good in each eye while trying to keep the eyes as straight as possible, hoping to keep them in alignment so that binocular vision can be achieved. He added that, in the particular group under discussion, orthoptics, when given at the proper age, has been helpful, but that it is rarely possible to give effective orthoptics under the age of six or seven years. He frankly stated that the passage of time is also a great factor in improving the situation for this group had recounted several cases in which he has observed the accommodation to improve markedly when the patients reach their teens. Unfortunately, he said, cases do not fit into nice little compartments and usually show mixtures so that one has to use variations of techniques on different cases at different times.

Dr. Costenbader then discussed the third group—those with an exaggerated response for any type of stimulation. These he called, "the hyper-reactors." He stated that they will probably show a high ratio of abnormal electroencephalograms, that these children are usually nervous and fidgity; that the onset of the strabismus is usually early, in many cases as young as six months. There is an

insignificant degree of hyperopia but the near-point is normal; binocular vision is unstable. Accommodation seems to be so organized that it takes a minimum stimulation to disturb it, and the patient does not have enough cortical control to enable him to handle the situation. It was also speculated that, possibly, the divergence mechanism is under par.

Miotics have been helpful, and bifocals to some extent. However, sedatives and anticonvulsants may help this group more than anything else. Orthoptics is definitely not worthwhile. With the passage of time, the tendency to strabismus gradually disappears.

Dr. Costenbader also discussed the use of miotics in strabismus in general. Pilocarpine must be used too often and frequently gives erratic effects but DFP, particularly for those with an abnormal accommodation-convergence ratio, is very helpful. However, the difficulty with DFP is largely in getting the proper strength. He has used a 0.24-percent strength once daily over periods of time varying from one month to two years. Some of the patients have developed iris cysts but, upon stopping the medication, these have disappeared. He has found three groups in which this drug has been helpful: (1) A small child of one or two years who takes about a +2.0D. sph. (if the DFP does not help this child, he immediately proceeds with surgery); (2) those who have had surgery and still have an inconstant tendency to converge; (3) frankly abnormal accommodation-convergence ratio.

It would be anticipated that this last-named group would be the one to benefit most but there are some patients in this group who get no effect whatever. There are others who get good effect as long as the DFP is in use but relapse as soon as it is discontinued, and another portion of this group will maintain the improvement after discontinuing the drug.

He concluded his paper by pointing up the purposes of his discussion: (1) To put intermittent esotropia somewhat into focus and to eliminate certain types that he did not want to discuss at this time; (2) under the so-called accommodative esotropia, he distinguished at least three factors that are thought to be significant—hyperopia, weakness of the accommodative mechanism and a hyper-responsive central nervous system.

Discussion. The discussion of the paper brought out the following points: Dr. Costenbader will not do surgery if the eyes are straight with glasses on. He will do surgery within three months after putting glasses on, and deciding that there is a large residual nonaccommodative element. He also operates those with a significant esotropia, even though the eyes are straight, if there is a tendency for the esophoria to become esotropia at times. He treats some youngsters who have had a squint for less than a week or two, by giving them +2.0 or more diopters of correction, and has noted that many of them progress to a constant esotropia in spite of further attempts at orthoptics. This group also is operated. In congenital esotropia he will operate the patient by the time he is one year of age, and states that he has been following this policy for over 10 years.

David H. Scott,
Recorder.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

March 17, 1955

Edmund B. Spaeth, *Chairman*

Diagnosis and treatment of limbus lesions

Dr. Charles E. Iliff, Baltimore, Maryland, discussed some interesting lesions of the limbus, including some tumors, some inflammatory lesions, and some degenerative changes, which have offered a problem either in diagnosis or in treatment. Emphasis

was placed on the clinical picture and, although the pathologic findings were not taken up in detail, it was suggested that the final weight of diagnosis lies here and the importance of a biopsy specimen cannot be overemphasized.

Differential diagnosis of limbal tumors is greatly aided by the knowledge of the age of the patient and the duration of the lesion. In children, benign tumors of congenital origin are most commonly noticed early in childhood, though some escape detection until puberty or even later. In adults, there is a very sharp increase in the frequency of malignancy. Thus, for practical purposes we can consider most limbal tumors in children benign, and in such cases therapy can be conservative. In adults, on the other hand, where a high percentage of the tumors are malignant, therapy must be more radical, making complete removal of the malignancy primary in importance.

The dermoid, angioma, nevus, melanoma, papilloma, and epithelioma offer special points of interest either in diagnosis or treatment. The method, using iodine for the removal of epithelial tumors which have not penetrated Bowman's membrane, was described in detail.

The treatment of some inflammatory limbal lesions, of pterygia, and of Mooren's ulcers was discussed. The success of the partial penetrating graft has altered the view of the prognosis of corneal ulcers. The possible use of frozen cornea was suggested, if fresh material is not available. The work being done in this field was briefly mentioned and slides were shown of a successful grafting of frozen material.

Discussion. Dr. John Finley: I remember a large dermoid cyst that Dr. Iliff treated. It involved the complete temporal region of the palpebral conjunctiva. I would like to ask the method of incision; I have had two cases like that.

Dr. Charles E. Iliff: I removed it by doing a lamellar keratectomy, going down to the clear cornea and then excising the whole lesion, and sliding the conjunctiva as much as I could laterally. In this lesion I also took conjunctiva from the other eye to cover the defect.

Dr. James S. Shipman: I would like to ask Dr. Iliff what technique he uses for ordinary pterygium and what particular knife?

Dr. Charles E. Iliff: I like the Gill knife. I think it gives the best splitting procedure that we can get, but I am perfectly happy to have you use any of the other knives that are used in ophthalmology. The Gill knife is a little cupped one that has a rounded, but very sharp, cutting surface, and one can split the lamella of the cornea. I use a Gill knife to outline the pterygium and remove it in toto whether it is small or large. I do not treat all of the cases with irradiation. For the little ones, I do not think it is necessary to use cortisone postoperatively but, if I notice any inflammation of vessels, I go ahead and use radiation.

Dr. I. J. Eisenberg: What kind of radiation? Is it always beta or gamma?

Dr. Charles E. Iliff: I use beta radiation from the Burman applicator, which is radon. It has a certain percentage of gamma but gamma is low compared to the output of beta.

Dr. Harold G. Scheie: Dr. Iliff, what changes have occurred in some of your patients that have had fairly large amounts of beta radiation? For example, I saw several patients of yours at Valley Forge Hospital in 1947 and 1948. Have any of those patients been followed and, if they have, what do they show today? I have never seen any.

Dr. Charles E. Iliff: Some of those have shown dilated vessels behind the squamous cells, such as occurs with radiation elswhere. I think they had too much treatment. I have not seen any of those break down in our group, but cases have been reported in which there is a certain amount of hyperplasia. The lesion is not as bad as I showed here but is a sloughing of superficial cells, such as you see with gen-

eral reaction of the eyes. We have had one patient who lost all her lashes. She was overtreated. It was one of the early cases; she had a scaling of her lids. Whether this was due to beta irradiation or to other factors as well I cannot say. The thing that we have noticed in the cases that we overtreated is the dilated matrix of vessels. You can tell a case that has been heavily treated.

William E. Krewson, 3rd,
Clerk.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

March 7, 1955

DR. FREDERICK H. THEODORE, *President*

BIOMICROSCOPY WITH POLARIZED LIGHT

DR. GEORGES KLEEFELD said his papers on this subject have appeared since 1938 in the *Bulletin de la Société belge d'ophthalmologie.* They have described many findings which could be elicited by the use of polaroids only.

The principles of polarization were demonstrated in the projecting lantern: polaroids in parallel and in crossed position; birefringence of calcite; birefringence in crystals (benzoic acid) and fatty acids, and stearic acid where, in addition, elliptic polarization can be elicited; diffraction and interference colors in mica between rotating polaroids.

The author succeeded in maintaining the transparency of a fish lens by preservation in a mixture of carbohydrates. This fish lens, between polaroids, shows the phenomenon of the black and of the white cross, which appear clearly on the screen.

According to Dr. Kleefeld, the black cross is characteristic of polarization in spheroids; he thinks that the polarization phenomena take place along the darkened areas only, whereas, in plane surfaces full extinction takes place.

He demonstrated that the phenomena observed in dioscopy can also be observed in episcopy, thus the possibility of examining details of the eye in incident polarized light; the polarizer should be movable circularly; the analyzer may be a pair of polaroid spectacles.

He showed his own paintings of the black and the white cross over the cornea, the disappearance of the Tyndall phenomenon in the anterior layers of the cornea, and in the nucleus of the lens—the appearance of birefringent bodies in the aging lens—the presence of birefringent bodies in the exudate of Kuhnt-Junius' disease.

He insists upon polarized and depolarized light as a means to detect reflecting surfaces.

He explains the Haidinger-brush factor as a cause of blurring of the image in the fovea exposed to a polarizing device. He believes that the Haidinger brush is due to dichroism in the funnel of the fovea.

The main object in biomicroscopy of the eye with polarized light is to view the behavior of the substances when met by polarized light—reflection, depolarization, elliptic polarization. Some structures and aspects can be elicited by this method only.

Discussion. DR. LUDWIG VON SALLMANN commented that he did not know enough about polarimetry to discuss the optical aspect of Dr. Kleefeld's paper but that he was aware of the great potentialities of this method of distinguishing various types of cataract and particularly of differentiating between different lesions in the macula. He would be grateful if Dr. Kleefeld would tell us more about his observations on Kuhnt-Junius macular degeneration.

Dr. Kleefeld replied that he was pleased to have Dr. von Sallmann's questions, and went on to say that thanks to his so-called "shadow-casting device" whose description is given in the *Bulletin de la Société belge d'ophtalmologie,* 1948, it is possible to study with greater exactitude the location, as well as, by their polarizing properties, the nature of opacities in the lens.

In Kuhnt-Junius disease, there is a glistening exudate. The infiltrated retina is pushed forward. In crossed polarized light, the reflection over the retina disappears and refringent isolated masses, as well as vessels, become conspicuous. It was possible to take photograph of these lesions by adding polaroids to the Nordenson's retinograph (*Bull. Soc. belge d'ophtalmologie*, 1939).

Dr. Joseph Pascal added that there is no question but that the use of polarized light can give interesting information not otherwise obtainable. Would it be possible to use the polarizing phenomena on the cornea to find a rise of intraocular pressure? He mentioned this because, a number of years ago, the late Dr. John Evans had an idea of developing an optical tonometer. Dr. Evans was convinced that the reflected image from the cornea showed some differences when the cornea was under normal tension and when the cornea was under increased tension. We know that stress and strain in a transparent substance, such as glass, produces double refraction and polarization phenomena. Possibly such phenomena take place in the cornea when it is under increased pressure, as in glaucoma, and perhaps by means of polarized light we could detect a difference in the degree of polarization and possibly a rise in tension.

Dr. Kleefeld replied that he highly appreciated the suggestion expressed by Dr. Pascal and that this will promote further observations on his part concerning possible changes brought about by glaucoma in the aspect of the cornea in polarized light.

The black-cross pattern can be observed in all cases of glaucoma, even in absolute glaucoma where the cornea is edematous and bullous. On the other hand, we should not forget that the black cross resolves itself into delicate, wavy, irregularly thick structures, which the polarizing microscope locates in the anterior two thirds of the lamellar tissue, the epithelium and Bowman's membrane appearing like ghost structures. It is possible that changes will be observed by improved methods. The same can be said concerning the colored patterns which extend like a square encasing the extremities of the arms of the cross.

Hemangiopericytoma of the orbit

Dr. Sidney A. Fox said that, to date, only 54 cases have been reported in the general medical literature. None has appeared in the ophthalmic literature.

According to the history this vascular tumor was first noted in the conjunctiva of the right external canthus of a 14-year-old white girl. In the next 20 years it had been cauterized, treated with radium several times, and resected three times. Three years after the last resection, it recurred again. At operation the tumor was found attached to the right external rectus muscle and the periosteum. It was resected in toto. Reaction to the operation was violent and followed by a diplopia which finally subsided in six months. A resultant symblepharon at the external canthus was corrected a year later. The final result was good.

Hemangiopericytoma is one of a small group of vascular tumors including the hemangioendothelioma and leiomyoma which unlike most vascular tumors has malignant tendencies. The hemangiopericytoma especially shows an aggressive tendency to recurrence.

Discussion. Dr. Arthur Linksz asked Dr. Fox whether motility improved after surgery. Dr. Fox replied that it is too early to tell this for at least three months and that there probably would not be complete motility. When you strip the sheath of the external rectus muscle, you cannot expect this. However, in the straight-ahead position, to the right, up and down, the patient is fine. There is also improvement to the left but it is not complete.

Unilateral sympathetic ophthalmia

Dr. Samuel Gartner stated that sympathetic ophthalmia is generally defined as a bilateral disease. It was indeed surprising to

him to have had a case that met the diagnostic criteria of sympathetic ophthalmia but was confined to only one eye.

A search of the literature revealed that this has been described before. E. Fuchs, in 1908, reported two such cases which he examined histologically. However, a criticism may be justified in that they were diagnosed before the use of the slitlamp, though it was universally recognized that E. Fuchs was an outstanding clinician and had made a great personal contribution in his studies of sympathetic ophthalmia.

Since then other cases of unilateral sympathetic ophthalmia have been described; most of them were studied with the slitlamp. Meller reported two such cases in 1915, and, in 1925, Marchesani described a unilateral case. In 1934, Felsenthal also reported a case; in 1950, Deavignes had two cases. In all these cases, the diagnosis was established by histologic study.

In the Russian literature in 1943, Kosena reported 70 unilateral cases out of 700 eyes enucleated for traumatic iridocyclitis. This is a surprisingly large number of unilateral cases. Since Dr. Gartner has only read the abstract and found no details in it, he cannot evaluate this study.

Sympathetic ophthalmia is a diagnosis that is usually based on the history of injury or operation, followed by inflammation of the eye and, within a relatively short time, by similar involvement of the second eye. The uveitis has specific histologic characteristics that establish the diagnosis. There is an inflammatory reaction in the uveal tract, consisting mainly of small round cells with perivascular cuffing, nodules of epithelioid cells, and frequently giant cells.

The inflammation is massive but practically limited to the uveal tract. In the choroid, the mass of inflammatory cells stays within its confines with the further limitation that the choriocapillaris is usually not affected. Only in the late stages do some extensions occur beyond these borders. There is an absence of necrosis, caseation, or tissue destruction.

A case of a man, aged 77 years, was reported. He never had any eye problem till two weeks before his first visit when the right eye became painful and inflamed. Vision became bad with the onset of the attack. When Dr. Gartner saw him for the first time on June 9, 1954, he had an acute glaucoma in the right eye with tension over 60 mm. Hg (Schiøtz). Vision was limited to light perception. The left eye had a tension of 18 mm. Hg, and, aside from a few lens opacities, appeared normal and had a corrected vision of 20/30.

Pilocarpine, eserine, and, later DFP were instilled. Diamox was given by mouth in doses of 500 mg. but the tension did not come down to any appreciable extent. He was hospitalized and, on June 14, 1954, an iridencleisis was performed. A shallow chamber reformed. On the fourth day he had a hemorrhage in the anterior chamber. The eye stayed congested and painful. The tension to fingers fell after operation but soon rose again. Two weeks after the operation, tension was 45 mm. Hg and, after that, rose to over 50 mm. Hg. Light projection became poorer. The eye was inflamed and painful. It was seven weeks after the iridencleisis when he accepted enucleation, which was performed on July 30, 1954.

The interesting feature is that his other eye never troubled him and clinically never showed any uveitis. Particularly after seeing the microscopic slides, Dr. Gartner repeatedly examined him at the slitlamp and never saw any inflammatory reaction.

The slides demonstrate the findings typical of sympathetic ophthalmia.

Slides were shown and Dr. Gartner pointed out the extensive uveitis, most marked in the choroid. There is massive round-cell infiltration, especially around the veins. There are nodules of epithelioid cells. The inflammatory reaction is typically in the choroid, with no involvement of the choriocapillaris. Giant cells were not found but they are not essential to the diagnosis, as they are often absent in the early cases.

This is a rare case of unilateral sympathetic ophthalmia. It may be that there was a long incubation period and the second eye was saved by enucleation. Another possibility that cannot be ruled out is that the second eye has had a subclinical involvement. However, it is seven months since the enucleation and the other eye shows no defect.

Discussion. Dr. Gerald B. Kara stated that there are several things one could say. Here he thinks we are justified in being doubting Thomases. He is never happy in making a diagnosis of sympathetic ophthalmia without microscopic verification. In this particular instance, some of the clinical criteria and, certainly, the slides presented are indicative of sympathetic ophthalmia. We can only assume that the remaining eye carried subclinical features of the disease. Then again, we are dealing with a problem in semantics. The very name indicates that bilateral pathology is present. Yet, here we have presented a unilateral case. We may have to modify our diagnostic criteria of sympathetic ophthalmia, if not the nomenclature.

Another possibility, though remote, is that this may be a case of lens-induced uveitis. In an eye sensitized to lens matter through previous surgery, a rupture of the lens capsule could produce this clinical picture. However, the microscopic findings are quite different. It is merely something to keep in mind. Before accepting Dr. Gartner's terminology, I would like to see the other eye.

Dr. Gartner replied that, as for Dr. Kara's wish to see the other eye, he hopes that eye stays well so he will not be able to show it to him. He is certain, however, that nobody can be completely sure of all the possible factors in this case unless the other eye is examined microscopically.

As for the possibility that this is lens-induced uveitis, he does not think so. He has seen a number of eyes in cases in which there was extracapsular extraction in one eye that developed cataract and uveitis in the other eye. That is a definite entity with rupture of the lens capsule and an inflammatory reaction in the iris and not the specific type of change in the choroid that we associate with sympathetic ophthalmia. In this case the lens may have been a factor in inducing the glaucoma.

Dr. Ludwig von Sallmann commented on the cases of Dr. E. Fuchs, whose observations were made before the use of the slitlamp, and said that he had had the privilege to work with Dr. Fuchs, who excelled in the use of the loupe.

Dr. Gartner replied that he was very much interested in Dr. von Sallmann's comments about the ability of Dr. E. Fuchs to use the loupe. He published slides of his cases and they certainly appeared to be cases of sympathetic ophthalmia.

Lymphosarcoma of bulbar conjunctiva

Dr. Benjamin Friedman reported the case of a 72-year-old Spanish lady who presented a rapidly growing lymphosarcoma limited to the bulbar conjunctiva. The growth was considered to be primary. Examination by systems failed to reveal any evidence of lymphosarcoma elsewhere in the body. Bone-marrow studies were negative. The condition responded dramatically to treatment with the Strontium-90 applicator.

Discussion. Dr. Max Chamlin remarked that, several years ago, he had a similar case but he was not quite as fortunate as Dr. Friedman was in the outcome. All that could be found was a mass in the orbit. An incision was made through the lower lid and it was possible to remove the mass. It turned out to be a lymphosarcoma of the orbit. Prior to the operation, detailed X-ray studies of all the bones, blood count, and sternal marrow puncture failed to reveal any evidence of lymphomatous disease. With the disclosure of the histopathologic nature of the tumor, radiotherapy was given locally. There was no local recurrence but, several months later, the patient developed typical lymphatic leukemia.

Dr. Frederick H. Theodore commented that he thought it always safer, when in doubt as to the diagnosis, to do a conjunctival biopsy rather than not to do one. It is entirely harmless if done carefully. It is amazing how often cases of the type presented are treated as inflammations for long periods of time before the true diagnosis is made. One such case recently came to his attention. This patient had proved lymphosarcoma of the stomach. Despite this, a diffuse and characteristic conjunctival lesion that appeared later was treated with all sorts of antibiotics, until a biopsy was done. I believe that biopsies of the conjunctiva should be done more frequently than they are.

Dr. Samuel Gartner remarked that lymphomas occasionally come to the attention of the ophthalmologist. The first diagnosis of lymphosarcoma and, later, the clinical picture change so the diagnosis becomes leukemia. They seem to have a common origin and go over into each other. The life expectancy of these patients may be quite long. He has followed some patients for over 15 years. A good many of them survive 15 to 20 years. The one-year survival of Dr. Friedman's patient is encouraging, but it does not, of course, put the patient in the clear. These tumors are radiosensitive and are, therefore, treated as soon as possible by local radiation.

Dr. Friedman replied that true lymphosarcomas which are primary in the bulbar conjunctiva are extremely rare. No doubt if we all pooled our experiences we might report on only a few cases in our collective lifetimes. On the other hand, the benign lesions in the fornices are relatively common. The biopsy of a benign lesion is not necessarily informative because, under the microscope, the potentially maligant tumor, before it has become activated, looks exactly like the benign growth. More careful recording on a large scale is essential to supply needed information. When a lymphosarcoma is amenable to surgery, it may be excised but, in the case of an extensive conjunctival lesion of this kind, surgery is much less simple than therapy by radiation.

Glioma of the optic chiasm

Dr. Jesse M. Levitt reviewed the clinical findings common to glioma of optic nerve and chiasm as a group, and pointed out the special features, diagnosis, and treatment of glioma originating in the chiasm.

He reported a case of a six-year-old girl with a history of progressive loss of vision and primary optic atrophy of both eyes manifesting itself at the age of two years and culminating in blindness. The only other symptom was frontal headache of recent onset.

Physical examination was negative except for a positive Macewen sign on head percussion. X-ray studies of the skull revealed sutural diastasis, deepened convolutional markings, a pear-shaped sella turcica, undermining of the anterior clinoids, and enlargement of both optic foramina. Ventriculography disclosed marked hydrocephalus and a large chiasmal lesion indenting the floor of the third ventricle.

At operation, a tumor was removed from the sellar region. It proved to be a fibrillary astrocytoma with ganglion cells, originating most likely in the optic chiasm.

Discussion. Dr. Max Chamlin said that Dr. Levitt's point about X-ray examination is well taken. Any patient with a history of progressive loss of vision and no abnormal findings in the media or fundus to account for such loss should certainly have X-ray studies made of the orbit and the skull, in addition to detailed field studies when possible. He was a little surprised to hear about the large number of gliomas reported in the literature. Despite the fact that a good many cases of this nature come to his attention, he did not remember more than two cases that had definite gliomas of the optic nerve.

Several months ago he was called in to see a girl, aged 11 years, with proptosis and optic atrophy in one eye. Visual fields sug-

gested a chiasmal lesion. The patient was believed to have a glioma in the region of the optic chiasm. While X-ray therapy seemed to control the condition for a while, eventually there was progression of the field defect and the patient was operated on. The lesion turned out to be a craniopharyngioma despite the fact that there was proptosis and that there was not any suprasellar calcification.

It would be Dr. Chamlin's impression that a glioma of the optic nerve or chiasm might be a little less common than the literature would have us believe, because some of the diagnoses are made without benefit of surgical verification.

Dr. Levitt replied that Dr. Don Marshall reported that he had collected 660 cases. Dr. Levitt had himself seen several cases and reported a few.

Jesse M. Levitt,
Recording Secretary.

Ophthalmic Miniature

In the other six eyes (aphakic glaucoma) in which no iritis or only very slight iritis occurred, the angle of the anterior chamber was found completely closed by the contact of the root of the iris with the periphery of the cornea. The advance in the position of the iris had been occasioned in five of the cases by adhesion of the lens capsule to the extraction scar. In the remaining case, in which the lens had been removed in its capsule, there was a similar adhesion of the anterior hyaloid membrane of the vitreous.

Treacher Collins,
Ophthalmological Society of the United Kingdom, 34:40, 1914.
Transactions of the

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*
700 North Michigan Avenue, Chicago 11

LAWRENCE T. POST, *Consulting Editor*
640 South Kingshighway, Saint Louis 10

ALAN C. WOODS, *Consulting Editor*
Johns Hopkins Hospital, Baltimore 5

BERNARD BECKER
640 South Kingshighway, Saint Louis 10

WILLIAM L. BENEDICT
100 First Avenue Building, Rochester, Minnesota

FREDERICK C. CORDES
384 Post Street, San Francisco 8

SIR STEWART DUKE-ELDER
63 Harley Street, London, W.1

EDWIN B. DUNPHY
243 Charles Street, Boston 14

F. HERBERT HAESSLER
561 North 15th Street, Milwaukee 3

PARKER HEATH
Sullivan Harbor, Maine

S. RODMAN IRVINE
9730 Wilshire Boulevard,
Beverly Hills, California

JAMES E. LEBENSOHN
4010 West Madison Street, Chicago 24

DONALD J. LYLE
411 Oak Street, Cincinnati 19

WILLIAM A. MANN
30 North Michigan Avenue, Chicago 2

A. EDWARD MAUMENEE
Johns Hopkins Hospital, Baltimore 5

P. ROBB MCDONALD
Lankenau Medical Building, Philadelphia 31

FRANK W. NEWELL
950 East 59th Street, Chicago 37

JOHN V. V. NICHOLLS
1414 Drummond Street, Montreal

ALGERNON B. REESE
73 East 71st Street, New York 21

PHILLIPS THYGESON
220 Meridian Road
San Jose 26, California

M. URIBE TRONCOSO
215 West 92nd Street, New York 25

KATHERINE FERGUSON CHALKLEY, *Manuscript Editor*
Lake Geneva, Wisconsin

Directors: WILLIAM L. BENEDICT, President; FREDERICK C. CORDES, Vice-President; WILLIAM A. MANN, Secretary and Treasurer; F. HERBERT HAESSLER, DERRICK VAIL, ALAN C. WOODS.

Address original papers, other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 700 North Michigan Avenue, Chicago 11, Illinois;* Society Proceedngs to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in *double space,* with wide margins.

Exchange copies of the medical journals should be sent to *Dr. F. Herbert Haessler, 561 North 15th Street, Milwaukee 3, Wisconsin.*

Subscriptions, application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 664 North Michigan Avenue, Chicago 11, Illinois.* Copy of advertisements must be sent to the manager by the 15th of the month preceding its appearance.

Change of address notice should be received not later than the 15th of the month prior to the issue for which the change is to go into effect. Both old and new addresses should be given.

Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Fifty reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Company, Inc., 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

INTRACRANIAL BRUITS*

Auscultation of the skull is often omitted from a neurologic examination, but Mackenzie, in a recent account of intracranial bruits, has drawn attention to the importance of this method of examination. Travers, in 1809-11, appears to have been the first to record an intracranial bruit, in a patient who in all probability had a carotico-cavernous fistula; and some years later Fisher made a number of observations on the "cephalic bellows sound." He found this sign in children with chronic hydrocephalus and congestion, acute inflammation, and compression of the brain, and he thought the bruit resulted from impediment to the free passage of blood

* Reprinted by permission from *The Lancet,* February 4, 1956.

through the basal arteries as they were compressed by the diseased brain against the bony channels in which they ran. In 1843 Whitney noted a bruit in an adult with an aneurysm of the basilar artery; and in 1898 Hoffman made the first presumptive diagnosis of an intracranial angioma when he heard an intracranial bruit in a patient with a spastic left hemiparesis.

An intracranial bruit may be hard to hear, and it should be listened for in quiet surroundings, which are often difficult to find in an outpatient department. It is often heard best over one or other eyeball, but auscultation should also be carried out over the temporal fossae and the mastoid processes.

The condition most commonly associated with an intracranial bruit (sometimes a very loud one) is a carotico-cavernous fistula, usually the result of trauma but sometimes due to spontaneous rupture of a carotid aneurysm into the cavernous sinus. A bruit can be heard in some intracranial angiomas, and it is perhaps in this condition that careful auscultation of the head is of most value.

The proportion of these patients in whom a bruit has been heard varies in different series:

Tonnis recorded it in only four out of 22 patients, but Mackenzie, in a previous study of 48 patients with intracranial angiomas proved by arteriography, recorded a bruit in 24. He made the interesting observation that a bruit was heard in 65 percent of the patients in whom the presenting symptoms were epilepsy, periodic headaches, or a hemiparesis, while it was uncommon in patients whose initial symptoms were a subarachnoid or intracranial hemorrhage. The importance of listening for a bruit is emphasized by two case records given by Mackenzie:

A patient, aged 23 years, had had minor epileptic attacks for seven years and two major attacks in the 15 months before she was seen at hospital, the only focal feature about the attacks being a transient aphasia at the onset; a bruit heard over the left eyeball indicated carotid angiography and this showed an angioma in and around the left Sylvian fissure.

Another patient had begun to have attacks of migraine at the age of 12 years; the visual aura was always on the right and the headache on the left. At the age of 26 she had a persistent defect in the right lower quadrant of the visual field. At the age of 41 years a bruit was heard over the left eyeball and left mastoid process, and arteriography showed a large left occipital angioma.

Mackenzie records the rare occurrence of a bruit with a noncommunicating intracranial aneurysm, a frontal meningioma, and a glomus-jugulare tumor, and for a short time in a patient with occlusion of the internal carotid artery.

The occasional presence of a bruit in children with raised intracranial pressure is well recognized, and Mackenzie mentions two cases of this kind; in one the pressure was raised by a pineal tumor and in the other by cerebral thrombophlebitis. He emphasizes that an intracranial bruit may at times be heard without any other indication of an intracranial lesion, and that the presence of a bruit does not in itself warrant further investigation. He refers to a patient in whom a bruit apparently due to a moderately severe anemia disappeared when the anemia was corrected.

Another unpublished observation is in keeping with this; a physician who had had two large gastro-intestinal hemorrhages heard a noise in his left ear which was synchronous with the pulse and which stopped completely on carotid compression; the noise disappeared when the anemia was corrected by blood-transfusion. Although it is not known whether this noise could be heard by an outside observer the patient described it as having the characteristics of an intracranial bruit, a sound with which he was familiar.

The site of origin of an intracranial bruit is usually considered to be the arteriovenous communication which occurs in carotico-

cavernous aneurysms and many intracranial angiomas, but Mackenzie suggests that another mechanism may be important in some cases. With intracranial vascular abnormalities there may be increased blood-flow through the carotid or vertebral arteries, and he suggests that, particularly in the carotid, there may be a relative stenosis where the artery enters the intracranial cavity. This may be the origin of the bruit, and it would explain why it may be heard most easily over the eyeball. A similar mechanism of relative stenosis of the basal arteries would explain the bruit in children with raised intracranial pressure—the explanation originally suggested by Fisher in 1838.

References

Fisher, J. D.: Med. Mag., Boston, **2**:144, 1834.
———: Am. J. M. Sc., **22**:277, 1838.
Hoffman, J.: Münch. med. Wchnschr., **2**:1159, 1898.
Mackenzie, I.: Brain, **76**:184, 1953.
———: Brain, **78**:350, 1955.
Tonnis, W.: Quoted by Mackenzie.
Travers, B.: Med.-chir. Tr., **2**:1, 1809-11.
Whitney, S. S.: Am. J. M. Sc., **6**:281, 1843.

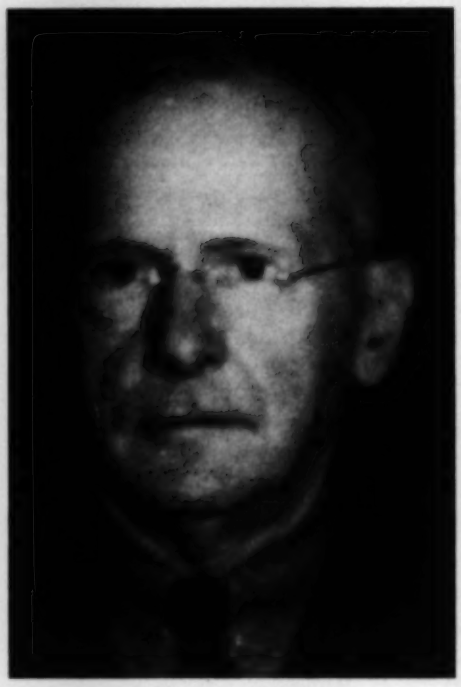
OBITUARY

HENRY COOPER HADEN

(1873-1956)

Dr. Henry C. Haden died at Houston, Texas, on April 24, 1956, following a long illness. He was born in Galveston on December 7, 1873, the son of Dr. John M. Haden and Sarah Brannum Haden. His father was a medical officer in the Confederate army and served for a while as the surgeon-general. Hanging in Dr. Haden's office was a plague signed by hundreds of citizens of Galveston in appreciation of his father's work in keeping yellow fever out of the city during an epidemic which devastated the surrounding country.

Henry Haden attended the Sewanee (Tennessee) military academy as a boy and it was there that he met and became a lifetime friend of Dr. Edward C. Ellett. He received



Henry C. Haden

the degree of doctor of medicine from the University of Pennsylvania in 1895 and worked as assistant to Dr. George deSchweinitz for several years. After a period of study in Vienna, he returned to Galveston as head of the Department of Ophthalmology and Otolaryngology at the University of Texas Medical School. In 1917, Dr. Haden entered the Army and became chief of the Division of Ophthalmology at Walter Reed Hospital, Washington. After the war ended, he moved to Houston where he practiced until his retirement.

Dr. Haden was president of the American Ophthalmological Society in 1947-48 and a member of all his local and state societies, as well as of the American Academy of Ophthalmology and Otolaryngology and the American College of Surgeons of which he was a founder member.

Dr. Haden's greatest interest, aside from the meticulous care he gave his patients, was

research on the embryology of the eye. He collected a great number of embryos through the years, had them sectioned, and studied them for his recreation. He produced many fine papers on this subject a number of which have been published in THE JOURNAL. He also wrote worthwhile contributions on the early diagnosis of glaucoma. Dr. Haden's fine collection of slides was left to the Department of Ophthalmology at Baylor University College of Medicine, in which he had taken great interest since the medical school moved to Houston in 1943.

Dr. Haden was a man one had to know intimately to realize the many kind and unselfish things he did, because he never spoke of them. I happened to be one of the fortunates that he took into his inner circle. The host of patients who mourned his retirement and death attest the affection and esteem held for him.

Dr. Haden was married to Blanche Randall in Trinity Church in Galveston, December 31, 1902, the church in which he was christened and confirmed and from which he was buried. He is survived by Mrs. Haden, a daughter, Mrs. Albert Bel Fay, and three grandchildren.

Everett L. Goar.

CORRESPONDENCE

AN AID TO TEACHING GONIOSCOPY

Editor

American Journal of Ophthalmology:

Occasionally, in teaching residents and other ophthalmologists the technique of gonioscopy, one encounters an individual who cannot fathom the three dimensional aspect of the angle when viewing it through a goniomirror or gonioprism. He just can't comprehend how in the mirror image the angle dips away over the last roll of the iris into the recess and then up again onto the trabecular zone.

In October, 1952, I presented at the meeting of the American Academy of Ophthalmology and Otolaryngology a series of ceramic models demonstrating the gonioscopic appearance of the angle in normal and pathologic conditions; these I hand-sculptured and painted to resemble the architecture of the angle. The models serve another purpose as well—in teaching gonioscopy I use them and Kodachromes of them to help the inexperienced gonioscopists better to understand what they see when viewing the angle through the mirror.

Some individuals still had difficulty. They knew the anatomy of the angle, and what they were supposed to see—yet could not understand what their eyes saw. To help them, I devised a simple gimmick which I think will enable them and other neophytes to understand gonioscopy.

A piece of thin white cardboard, rectangular in shape and measuring about 5 by 11 inches, is obtained. About two inches from one long margin there is painted with crayons, inks, water colors, and so forth, lines and zones to represent the trabecular zone bisected by the canal of Schlemm and limited above by the white line of Schwalbe and below by the brown ciliary zone; the distance between the Schwalbe line and the ciliary zone is about one inch on the cardboard; appropriate colors are used to help visualize the area; the bottom part of the "trabecular zone" can be lightly stippled to suggest pigmentation. Then the cardboard is rolled into the shape of a cone whose ends are approximately 3.5 and 2.5 inches in diameter, the larger end being where the "trabecular zone" had been painted; the markings are on the inside of the cone. Fasteners make the cone secure and permanent.

A child's small balloon, perferably in a light green or blue color, is partially inflated and inserted into the wider mouth of the cone with the neck of the balloon toward the small end. The top of the balloon will represent the anterior surface of the iris. Thus we now have the component parts of the angle of the anterior chamber with the

balloon the "iris," where the balloon fits next to the cardboard the "recess," and the painted part of the cardboard as the "trabecular zone, cornea, and so forth."

The balloon is positioned so that, when one looks into the larger end of the cone, he can see all the trabecular markings on the cardboard—thus the normal wide angle. By pressing on the inferior part of the cone, or the lower part of the balloon, the air pressure pushes the "iris" forward onto the "trabecular zone," obscuring some of the markings and creating thereby the gonioscopic view of a narrow angle. With additional pressure on the balloon, the "iris" is pushed forward further so that only the "white line" or the "cornea" will be visible, as in a very narrow closed angle. Unequal pressure on the bottom part of the cone will close one part of the "angle" and leave the rest normally wide.

This simple technique has been demonstrated to experienced, as well as inexperienced, gonioscopists. They were unanimous in the belief that it will greatly simplify and clarify the understanding of the gonioscopic view of the angle. Their enthusiasm prompts me to report this simple expedient for others to use in teaching of gonioscopy.

(Signed) Arthur Shainhouse,
Brooklyn, New York.

BOOK REVIEWS

ADVANCES IN OPHTHALMOLOGY: VOLUME 5. Edited by E. B. Streiff. Basel, S. Karger, A. G., 1956. 320 pages, 65 figures, some of them in color. Price: Swiss francs, 39.50.

Volume 5 of this admirable series was originally designed to embrace six papers but, because they each turned out to be longer than anticipated, only three of them appear in the present volume. The other three will shortly be published in Volume 6. Those who have the good fortune of obtaining and reading the first four volumes will hasten to avail themselves of the treat in store for them by getting this volume and ordering the next.

The present volume contains:

(a) An original paper on the early uveal and retinal vascular lesions in tuberculous infection, by R. Dufour of Lausanne, Switzerland (in French). This is a most informative discussion of 53 pages, beautifully illustrated and organized. It is most helpful in clarifying our thoughts on ocular tuberculosis, about which there is much confusion.

(b) A discussion of the cytologic aspects of the crystalline lens: a critical review and an outlook on future developments, by J. E. A. van den Heuvel of Groningen (in English). This is a treatise on the morphologic and histologic aspect of the lens in health and disease.

(c) A splendid and most comprehensive review of the literature on the uvea for the years 1946-1953, by J. François and E. De Vos of Ghent, Belgium, 107 pages (in French). The topics covered are embryology, anatomy, physiology, biochemistry, pharmacology and experimentation, the hereditary and degenerative diseases, choroidal degeneration, and uveitis.

Volume 6 will contain (1) a paper on keratoplasty with paraffin material by E. Bürki of Basel (in German), (2) ocular motility by P. A. Jaensch of Essen (in German), and (3) cornea and sclera: a review of the literature from 1946 to 1951 (second part) by S. Forni of Geneva (in French).

These books are excellent literary tools for the busy ophthalmologist.

Derrick Vail.

THE STORY OF BLINDNESS. By Gabriel Farrell. Cambridge, Harvard University Press, 1956. 270 pages, bibliography, index. Price: $4.50.

Farrell, director of the Perkins School for 20 years, tells the story of blindness in vivid, fascinating detail. The eminence attained by some exceptional blind persons in years past without the aid of braille, talking books,

guide dogs, and interested agencies is indeed a tribute to the indomitable spirit of man. Among the notable are Didymus, teacher of St. Jerome; Nicholas Saunderson, protege of Newton, professor of mathematics at Cambridge and lecturer on optics; François Huber, in his day the highest authority on bees; and William Prescott, the great American historian. Diderot first wrote on the problem of blindness; Rousseau called for action; and Valentin Haüy responded with the first school for blind children. In America, the education of the blind was developed by a great triumvirate, the directors of the schools in Boston, New York, and Philadelphia.

Samuel Gridley Howe, the first head of the Perkins School (1831), adopted as his guiding principle that the blind could and should contribute to society. His wife, Julia Ward Howe, wrote the famed *Battle Hymn of the Republic*. Dickens visited the school in 1842 and was so impressed by the attainments of the blind deaf-mute, Laura Bridgman, that he devoted 14 pages to her in his *American Notes*. A mother read this account 40 years later and through the Perkins School secured Anne Sullivan to train her six-year-old daughter, Helen Keller. The American Foundation for the Blind, in 1946, set up a program for the deaf-blind entitled the Helen Keller Department. The New York Institution for the Blind, under Wait, shifted the emphasis from craft training to academic instruction. One of its teachers was Grover Cleveland. The first day classes for the blind in the public schools was launched in Chicago in 1900; now 26 percent of blind children are thus educated.

World War I sparked definite programs for the rehabilitation of the blind. England led with St. Dunstan's, a voluntary agency founded by a dedicated semiblind journalist, Sir Arthur Pearson. In the Korean conflict seven percent of all casualties lost their sight, the highest ratio in any war. The government's annual toll for war-incurred blindness is 20 million dollars ($300 per month to 5,024). The grants for research in blinding diseases is less than one percent of this figure.

The blind of the world number 6.6 millions. The highest incidence (four per 100) is in the Jinja area of the Nile as a consequence of onchocerciasis transmitted by the buffalo gnat. Elimination of the blindness that is preventable would reduce the blind population of the future by over 50 percent. This objective is, in the words of Farrell, a challenge to the social conscience of the world.

James E. Lebensohn.

GEOMETRICAL OPTICS. By L. C. Martin, D.Sc. New York, Philosophical Library, 1956. 215 pages, 131 figures, index. Price: $7.50.

This text by a former professor of technical optics at the London Imperial College of Science and Technology provides a sound foundation for the aspiring specialist in optical science. The reader is assumed to be well versed in mathematics including analytical geometry and elementary calculus. Due emphasis is placed on the relation of the subject to practical problems and each chapter is accompanied by a set of exercises. The historical aspects are briefly touched and the illustrative figures include reproductions from Kipler, Descartes, and Huygens. Ametropia, aphakia, vertex refraction, and astigmatism are considered, but in a cursory manner only.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Mawas, M. J. **Origin, development and histologic significance of the fixed cells of the human iris and their relationship to iris tumors.** Bull. et mém. Soc. franç. d'opht. **68**:306, May, 1955.

The so-called fixed iris cells are not of mesodermal but of ectodermal origin and have melanoblastic capacities.

Alice R. Deutsch.

Suzuki, A. **Histology of normal human conjunctiva and electron microscopy of ultra-thin sections.** Acta Soc. Ophth. Japan **60**:441-459, June, 1956.

Suzuki studied the normal human conjunctiva by electron microscopy of thin sections to learn whether there are findings in the normal conjunctiva which should be differentiated from trachoma inclusions. (This study thus constituted the base of the study entitled "electron microscopy of trachoma virus in section" by Mitsui and Suzuki published in the AMA Arch. Ophth.)

On the screen of the microscope, mastcells, leucocyte granules, and the Golgi apparatus of the nucleus have some resemblances to trachoma inclusions but the former can easily be differentiated from the latter by photography. Mitochondria and initial bodies of trachoma should be carefully differentiated from each other on the photomicrograph. (26 figures, 13 references)

Yukihiko Mitsui.

Wudka, E. and Leopold, I. H. **Experimental studies of the choroidal vessels.** A.M.A. Arch. Ophth. **55**:605-632, May, 1956.

This extensive article is adapted from a thesis for a Master's degree in Ophthalmology. A historical review and a detailed description of the present-day methods of anatomical investigation are presented as a prologue to the authors' anatomical observations. Their primary objective was to outline the appearance of the choroid in the living animal. Findings are comparable to those in man because of the uniformity of mammalian choroidal characteristics. The authors' findings lend support to the view that there is no direct arterio-venous anastomosis in the choroid. (17 figures, 142 references) G. S. Tyner.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Coulliaud-Maisonneuve, M. **Culture of the Koch-Weeks bacillus.** Arch. d'opht. **15**:846-849, 1955.

The author reviews the literature on the cultivation and identification of the Koch-Weeks bacillus, referring especially to the studies of P. Durand at the Pasteur Institute of Tunis, and of D. Davis and M. Pittman of the National Institutes of Health. She then reviews her own studies on cultivation and recommends for isolation an agar medium containing beef heart infusion and red blood cell extract. On this medium 23 strains of the organism were obtained in 51 attempts.

P. Thygeson.

François, J., Wieme, R. J., Kaminski, M. and Rabaey. **A study on lens antigens by immunochemical methods of protein fractions.** Bull. et mém. Soc. franç. d'opht. **68**:144-158, May, 1955.

This very interesting study disclosed several important details toward a better understanding of the composition of the lens-proteins. The techniques used on extracts of beef lenses were double diffusion in a gelatinous medium and immunoelectrophoresis. At least eight different antigens were found and they were named by different letters, according to the order of their appearance and their electrophoretic fraction. Only minute quantitative differences could be shown between the extract of the cortex and the extract of the nucleus. Electrophoretic fraction I corresponds with the α-crystalline. It is organ specific since it was precipitated when the anticrystalline immune serum was added to lens extract of other animals. All the other fractions are only species specific. (7 figures, 17 references)

Alice R. Deutsch.

Niedermeier, S. **The importance of vasoneural correlations in the pathogenesis of endogenous ocular inflammations.** Klin. Monatsbl. f. Augenh. **128**:438-451, 1956.

In a series of animal experiments a piece of metal was implanted into the ciliary body of one eye. After four weeks a certain vasoconstriction with altered permeability of the vascular walls was noted in the other eye. In addition a nonspecific inflammation was produced in the second eye (in 10 out of 23 rabbits) when a toxin (tuberculin, tonsillar extract) was injected into the tonsils of the animal. These inflammations could be suppressed with steroids. Certain similarities with sympathetic ophthalmia are discussed. (6 figures, 60 references)

Frederick C. Blodi.

Siliato, Francesco. **The effect of anti-reticulo-endothelial cytotoxic serum on scar formation of experimental corneal wounds.** Ann. di. ottal. e clin. ocul. **81**:579-586, Dec., 1955.

Experimental penetrating wounds of the cornea showed more active scar repair in animals treated by intradermal injections of anti-reticulo-endothelial cytotoxic serum (serum of Bogomoletz) (8 figures)

John J. Stern.

Tomila, V. and Forsius, H. **Bacteria appearing in conjunctivitis and dacryocystitis and their sensitivity to antibiotics.** Acta Ophth. **34**:133-139, 1956.

Attention is called to the disparity of the reports in the literature in this field. The author's material consisted of 60 patients with various types of conjunctivitis, and dacryocystitis, and bacteriologic studies were made from the eyes and nose. Pathogenic bacteria were isolated in 39 cases, and Micrococcus pyogenes aureus was the most common organism found. Streptococcus pneumonia was second in frequency, but dominated the picture in dacryocystitis. The sensitivity

varied greatly in the different types of bacteria and in their strains, and it is concluded that the effective antibiotic can not be determined from the type of bacteria, and that resistance determination is indispensable as a therapeutic guide. Positive findings in samples from the nose show that in conjunctivitis and dacryocystitis the nose should be examined as well as the eyes. Attention is called to the fact that these data are essentially those of Finland, and may not apply to other countries. (4 tables, 5 references) Ray K. Daily.

Wilczek, M., Feltynowski, A. and Przybylkiewicz, Z. **Electron microscope investigation of trachoma virus.** Klinika Oczna. **25**:81-84, 1955.

Material collected from 17 eyes with second-stage trachoma was prepared according to the method of Cox. Three sizes of particles were found; all of them were spherical or oval. The sizes in millimicrons were 50 to 80, 150 to 300 and 450 to 500. Control studies of bacterial conjunctivitis did not show similar particles. (8 figures, 1 table, 3 references)
Sylvan Brandon.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alaerts, L. **Variations of the glucose content of the human aqueous.** Bull. et mém. Soc. franç. d'opht. **68**:46-50, May, 1955.

The aqueous of normal eyes in normal individuals has a more or less uniform glucose content which is considerably lower than that of the blood and independent of its variations. In diverse inflammations of the eye the amount of glucose in the aqueous increases, irrespective of the amount of glycemia or the presence of diabetes but dependent on various local, inflammatory, exudative, and degenerative changes.
Alice R. Deutsch.

Alagna, G. and d'Aquino, S. **Ocular changes from cobalt chloride.** Arch. di ottal. **60**:5-29, Jan.-Feb., 1956.

The hepatic, splenic and ocular changes produced by cobalt chloride were studied in rabbits and rats. Fibrosis and cirrhosis of the liver and hyperplasia of the spleen turning into cirrhosis were observed. The ocular changes are characterized by cataracts—similar in certain aspects to alloxan cataract—and degenerative processes of choroid, retina, and optic nerve. Administration of cystein inhibits or at least attenuates the hepatic and ocular signs. The changes caused by cobalt chloride are assumed to be attributable to an upset of enzymatic activities and of the function of the thiole group. (10 figures, 56 references) John J. Stern.

Back, Marcel. **Transient myopia after use of acetazoleamide (Diamox).** A.M.A. Arch. Ophth. **55**:546-547, April, 1956.

A patient taking acetazoleamide (Diamox) and on a salt-free diet for obesity, developed a transient myopia on the drug. The myopia could be reproduced by intermittent administration of the drug. (2 references) George S. Tyner.

De Conciliis, U. **The blood-aqueous barrier, the ocular fundus and the retinal respiration in acute and chronic hypoglycemia.** Arch. di Ottal. **60**:31-44, Jan.-Feb., 1956.

Hypoglycemia was induced in rabbits by insulin injections. In acute cases, the permeability of the blood-aqueous barrier was increased and the fundi showed dilated veins and hemorrhages. These same changes were more evident in the chronic form where they were accompanied by opacities of the lens, decreased retinal respiration and vitreous hemorrhages. These ocular manifestations of the hypoglycemic coma are attributed to a mechanical factor (muscular contractions) and to a vasodilator action of insulin. In

chronic hypoglycemia there is added a disorder of the "glyco-lipo-protein metabolism." (1 figure, 2 tables, 112 references) John J. Stern.

Dejean, C. and Paycha, F. **The results of chemical analysis of the aqueous in ocular diseases of various etiology.** Bull. et mém. Soc. franç. d'opht. **68**:58-65, May, 1955.

Investigations on the chemistry of the aqueous included evaluation of its albumen and chloride content. The normal albumen content is 0.20 gm. percent; the normal chloride content 7.6 to 10.3 gm. percent. The elements of the aqueous only undergo variations in uveal disease. The albumen increases in the presence of inflammation. The chlorides diminish in pathologic conditions and increase again during the period of recovery. Their determination has a certain prognostic value.

The tracing of radioactive bisodium phosphate inside the eyeball is described; 30 microcuries of P32 per kg. as injected into the marginal ear vein of rabbits and the changing P32 content of the blood and the aqueous were charted. The radioactivity of the aqueous could be demonstrated immediately after the intravenous injection. It achieved its highest point between the fifth and fourteenth hour, and was proportional to that of the serum. The radioactivity of the serum then diminishes because of fixation of P32 in the muscles, bones and nerve tissues. This type of examination promises to be of considerable help in future research on the physiopathology of the globe.

Alice R. Deutsch.

Dische, Z., Borenfreund, E. and Zelmenis, G. **Changes in lens proteins of rats during aging.** A.M.A. Arch. Ophth. **55**:471-483, April, 1956.

The authors' data indicate that the aging of the lens is associated with the continuous net oxidation of cysteine to cystine in lens proteins with continuous precipitation of albuminoid. This process is considered analagous to the keratinization of epidermis. (1 figure, 4 tables, 8 references) George S. Tyner.

Dische, Z., Borenfreund, E. and Zelmenis, G. **Proteins and protein synthesis in rat lenses with galactose cataract.** A.M.A. Arch. Ophth. **55**:633-642, May, 1956.

Rats fed on a galactose diet show up to 100 percent inhibition of synthesis of soluble proteins. The protein changes are probably important in the formation of vacuoles in the lenses of human eyes. (2 tables, 8 references) G. S. Tyner.

d'Ermo, M. F. **The technique of paper-micro-electrophoresis with minimal quantities of normal aqueous.** Bull. et mém. Soc. franç. d'opht. **68**:65-72, May, 1955.

The method described promises to be especially useful with very small amounts of material, or very low concentration of protein in a given liquid. It consists of the application of a small square of cellophane on the partition line of the filter paper promoting the resorption of the substance on the cellophane by the filter-paper without the use of pipettes and syringes, methods which always cause a certain loss of material. With this technique the various protein fractions can be made visible after staining and easily compared with those of the serum. (26 references, 3 figures) Alice R. Deutsch.

Franceschetti, A., Falbriand, A., Zender, R., Sanz, M. C. and Glocher, B. **The action of Diamox on specific electrolytes of the aqueous.** Bull. et mém. Soc. franç. d'opht. **68**:73-78, May, 1955.

The effect of Diomax on the sodium and potassium content of the aqueous was investigated. Twenty rabbits were used in these experiments. The Diomax

was given intravenously, 100 mg./kg. in 2 cc. of physiologic saline solution. The control animals got 2 cc. of physiologic saline solution; 0.1 cc. of aqueous proved to be sufficient to evaluate the sodium and potassium content on the flame spectrophotometer. The analysis was done before the injection of Diomax and three hours thereafter, using the other eye for paracentesis. While the control animals showed only a slight decrease in the potassium content, the injected animals all had a considerable reduction of potassium. These findings were thought to be significant for the evaluation of the action of Diamox. (16 references, 4 figures) Alice R. Deutsch.

François, J. and Rabaey, M. **New investigations on the physico-chemical properties of the mucoids of the cornea.** Acta Ophth. **34**:45-62, 1956.

This is a detailed report of a laboratory study on rabbits. The technique of corneal staining is described and it is pointed out that organic solvents and fixatives affect the swelling power of mucoid. It was found that a large amount of corneal mucoid prevents the penetration of blood-vessels into the cornea. The swelling of the corneal stroma is dependent on the pH, and at physiological pH the swelling depends upon the mucoid, the collagen fibrils playing no part. Cortisone has no effect on swelling of the corneal stroma, but concentrated protein solutions, such as serum and five percent albumin deter to a marked degree corneal swelling. Such solutions should be useful in corneal trauma. One is impressed in the laboratory, as well as in the clinic, with the important role which the corneal epithelium and Descemet's membrane play in the inhibition of the water content of the corneal stroma. (11 figures, 10 tables, 11 references) Ray K. Daily.

Heinzen, M. H. **The effect of Diamox on the transfer of radioactive sodium (Na24) through the blood-aqueous barrier.** Bull. et mém. Soc. franç. d'opht. **68**:79-82, May, 1955.

Heavy water and Na24 in a dose of about 600 microcuries and diluted in physiologic saline solution were injected into the peritoneal cavity of rabbits. Aqueous and blood were examined at predetermined intervals and the results were tabulated. A characteristic accumulation of Na24 was detected in the anterior chamber. The highest concentration was found after about 120 minutes; after about 50 to 60 minutes about half of the concentration was reached. The pattern was similar in all normal animals. After several weeks 500 mg. Diamox was injected intravenously into the same animals. The previous experiments were repeated. No change in the accumulation of Na24 in the anterior chamber was found, when compared with the tracing without Diamox. These findings were confirmed when the amount of nonirradiated sodium was registered on the flame photometer. Alice R. Deutsch.

Hellstroem, Bo E. **Experimental approach to the pathogenesis of retrolental fibroplasia: influence of the state of nutrition on oxygen-induced changes in the mouse eye.** Acta Paediat. **45**:43-57, Jan., 1956.

Although the work of Patz, Ashton and others has proved rather conclusively that retrolental fibroplasia is a consequence of oxygen poisoning in the premature infant, it has been felt by some workers in the field that the state of nutrition of the infant played a role in the development of this disease. In order to study this factor systematically Hellstroem exposed groups of mice to high concentrations of oxygen and then underfed some and overfed others. The underfed group showed less vascular proliferation in the retina, apparently because of generalized reduc-

tion of metabolic activity and need, while the overfed group definitely showed an increased proliferation of retinal vessels similar to that seen in clinical retrolental fibroplasia.

Although it is always dangerous to extrapolate experimental data to clinical conditions this fine paper would seem to indicate that deficiencies in the nutritional state play no role in the etiology of retrolental fibroplasia. (7 figures, 3 tables, 21 references) David Shoch.

Horsten, G. P. M. and Winkelman, J. E. **A new method of electroretinographic investigation for determination of the sensitivity of the retina. Phenomenon of electroretinographic exhaustion.** Ann. d'ocul. **189**:165-173, Feb., 1956.

A new electroretinographic phenomenon is investigated which is called "phenomenon of exhaustion." In this phenomenon, a rapid decrease of the b potential is observed on stimulation with repeated flashes in retinas under the influence of anoxemia. An explanation of this phenomenon is presented. (6 figures, 8 references) John C. Locke.

Kuebler, E. and Ruegg, J. C. **Fluoresceine diffusion into the anterior chamber of rabbits after excision of the superior cervical ganglion.** Klin. Monatsbl. f. Augenh. **128**:410-413, 1956.

The permeability of the blood-aqueous barrier increases after the excision of the superior cervical ganglion. This lasts for six or eight days and does not vary with the sensitization of the dilator muscle to adrenaline. (3 figures, 1 table, 8 references) Frederick C. Blodi.

Lieb, W. and Pirch, H. **Comparison of the effect of parasympathomimetic drugs.** Klin. Monatsbl. f. Augenh. **128**:593-604, 1956.

The effect of these drugs on the pupil, the accommodation, and the intraocular pressure was tested in 162 healthy persons. The effect increases from Doryl to pilocarpine, prostigmine, eserine, Mestinone and DFP. An increase in the concentration does not necessarily mean an increase in effect. The vehicle is of greatest importance. Unpleasant side effects decrease the usefulness of the phosphoric acid esters. (12 figures, 40 references) Frederick C. Blodi.

van Lint, A. and Alaerts, L. **The regulating mechanism of the ciliary muscles in accommodation and in intraocular pressure.** Arch. d'opht. **16**:44-53, 1956.

The authors discuss the mechanisms which govern the action of the ciliary muscles in accommodation and in connection with ocular tension. The theories of accommodation are reviewed and that of Helmholz is considered to accord best with known facts. After considering the Helmholz theory in detail, the authors conclude that accommodation results from the simultaneous contraction of the muscles of Müller and Bruecke, but in different amplitudes. They point out the varying degrees of development of these muscles, Bruecke's muscle being poorly developed in hyperopes and hypertrophied in myopes, Müller's muscle being just the reverse. They discuss the innervation of these muscles and the various effects of miotics and cycloplegics on them, in relation to both accommodation and ocular tension. They mention that pilocarpine and eserine, by provoking a hyperaction of the muscle of Müller, relax Bruecke's muscle by reflex action and diminish the intraocular pressure. They state that atropine, in paralyzing the first muscle, produces a hyperactivity of the second and a rise in pressure. They express the opinion that fistulizing operations which section the scleral spur (i.e., the circular tendon of Bruecke's muscle) owe a part of their pressure-reducing action to this effect on the muscle. Mechanisms by

which muscle action may influence pressure, e.g., vasodilation and vasoconstriction, are discussed. P. Thygeson.

Manna, Feliks. **Changes in serum protein level in treatment of eyes with typhoid vaccine.** Klinika Oczna **25**:103-112, 1955.

The serum protein level was determined in 45 patients before and after injection of typhoid vaccine. After the first injection there was a slight increase of protein which coincided with the presence of fever. There was also a considerable increase of globulin and a decrease of albumin. After the second and particularly after the third injection the protein level was lower. The changes in the protein level were in the proportion of globulin and albumin and had no relation to the effectiveness of the treatment. The author explains the lower protein level by the stimulation of formation of ACTH and steroids. The increase in globulin is ascribed to the stimulation of the reticuloendothelial system. (3 tables, 13 references) Sylvan Brandon.

Miller, H. A. and Andoneineix. **The diastolic retinal arterial pressure and chlorpromazine. (4560R.P.)** Bull. et mém. Soc. franç. d'opht. **68**:220-230, May, 1955.

The effects of different therapeutic agents, medical and surgical, on the general arterial blood pressure (P.A.H.) as compared to the retinal arterial (P.A.R.) bloodpressure were investigated by the authors in previous papers. They also studied the interesting relationship between sleep, blood pressure and retinal circulation. The authors had found that chlorpromazine (4500R.P) lowered the tension of the non-narcotized rabbit and analysis of their experiments proved that chlorpromazine does not have any antisympathetic action and very little effect on the parasympathetic. Its ganglioplegic action also is minimal, therefore it was concluded that chlorpromazine acts on the central nervous system. It seemed interesting to verify these findings in clinical investigation and to compare the results with the ones obtained with the "cure de sommeil."

Thirty-one patients were investigated, 23 of whom had had the induced sleep treatment and five a sympathectomy. Chlorpromazine was given intravenously, 0.5 mg./kg. in 5 percent dextrose. Care was taken not to give more than 100 cc. of fluid and to limit the infusion time to 30 to 50 minutes. Brachial and retinal arterial blood pressure (P.A.H. and P.H.R.) was registered every 10 to 15 minutes and during the critical period every 2 to 4 minutes. Chlorpromazine lowered the P.A.H. and the P.A.R. but showed a certain dissociation in the intensity of its action. The hypnotic effect of chlorpromazine was not always in accordance with the hypotensive effect. In spite of the fact that it promotes sleep, its action should not be identified with the action of the barbiturates. (3 figures, 2 tables) Alice R. Deutsch.

Montagne, F. **Utilization of a new derivative of dicoumarol in thrombosis of the retinal veins.** Arch. d'opht. **15**:850-853, 1955.

Under the trade name of Marcoumar (Roche), a derivative of dicoumarol offering the advantage of prolonged action has been tested. As an antidote in case of hemorrhage, vitamin K_1, under the name of Konakion (Roche), was kept in reserve but did not have to be used. In two cases the patients were treated with heparin for the first two days, and then with Marcoumar. During treatment the prothrombin level was controlled by the test of Quick. In both cases a final vision of 0.4 was obtained. Charts illustrating the prothrombin levels in the two cases during treatment are included. Levels from 22 to 35 percent were obtained dur-

ing the 3-week periods of treatment. The new drug is recommended.

P. Thygeson.

Politzer, G. **Experimental study of the development of Roentgen-ray cataract.** Arch. f. Ophth. **157**:459-472, 1956.

A single exposure of 14-day-old salamander larvae to 400 r of radiation results in disintegration of the lens in three months. The fibers swell and the capsule bursts near the anterior pole. One of the factors which brings about these changes is the loss of cells in the epithelium as a result of pathologic karyokinesis. In adult mammals similar changes occur at the anterior pole, there is much lens swelling, and typical posterior cortical cataract develops. In man and in the rabbit a single radiation up to 400 r is surely safe and in fractional radiation 400 r can be greatly exceeded. The author makes some suggestions for the prevention of occupational cataract in the roentgenologist. (8 figures, 22 references) F. H. Haessler.

Remky, H. **The aqueous-serum chlorine partition and its significance in the water metabolism of the eye.** Arch. f. Ophth. **157**:506-521, 1956.

This partition was determined in 404 cases and in some of them the author also measured the rate of increase in the aqueous, of fluoresceine which had been injected intravenously. The findings were also compared with data on the partition of sodium and fluoresceine reported by other investigators and also with published measurements of the entrance of Cl^{38} and Na^{24} into the aqueous. It was made clear that Cl and Na are actively transported and not dependent on the protein content. It is probably a secretory process in which the serum level of the substance is the determining factor. The source of energy of the secretory transfer may be the supply of ions through the blood-aqueous barrier. The correspondence between the Cl partition and the concentration rate of fluoresceine indicates that there can be only a direct relationship between Cl partition and glaucoma. An increase of Cl content of the aqueous over the serum can be accepted as a measure of an increased minute-volume. (8 figures, 8 tables, 24 references)

F. H. Haessler.

Sampaolesi, Roberto. **The diffusion of fluorescein into the vitreous body.** Arch. oftal. Buenos Aires **31**:55-58, Feb., 1956.

In 35 aphakic, but otherwise normal eyes, the diffusion of fluorescein into the vitreous body was studied by means of the well-known Amsler and Huber permeability test. In 26 eyes the drug was detected in the vitreous only after a five-minute delay with respect to the moment when it first appeared in the anterior chamber; besides, its maximum concentration remained slightly below that reached in the aqueous humor. In six the latent time of appearance and the concentration were the same in both media while in the remaining three the titer was somewhat higher in the vitreous than in the aqueous during the first 30 minutes. The results obtained in the two latter groups seem to support the view that the drug enters the vitreous body directly through the blood-aqueous barrier instead of merely diffusing back from the previously colored aqueous humor. (8 figures, 6 references)

A. Urrets-Zavalía, Jr.

Shibata, T. **The concentration of radioactive phosphorus (P^{32}) in blood and intraocular tissues after its intravenous injection.** Acta Soc. Ophth. Japan **60**:140-146, 221-216, 310-314, and 394-399, March, April, May, and June, 1956.

Radioactive phosphorus increases gradually in the iris and ciliary body after an intravenous injection of the tracer. It takes one hour to reach the climax and

then the tracer decreases gradually. Shibata considers, therefore, that the blood circulation in the ciliary body and iris is slow and the phosphorous metabolism sluggish. The concentration of the tracer in the choroid is considerably lower than that in the iris and ciliary body and there is no such increase of the tracer for the first one hour as in case of the latter. The concentration in the vitreous is extremely low.

He also studied the influence of some medicaments on the tracer concentration in ocular tissues. He found that the blood circulation and the phosphorous metabolism in the iris and ciliary body are accelerated by pilocarpine and retarded by atropine and epinephrine. (8 figures, 13 tables, 62 references)

Yukihiko Mitsui.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Bier, Norman. **A study of the cornea in relation to contact lens practice.** Am. J. Optometry **33**:291-304, June, 1956.

In a series of about 300 cases, the author found the thickness of the cornea varied from 0.5 to 1.0 mm. in the center and from 0.8 to 1.70 mm. at the limbus. The contour of the normal cornea was spheric in the regular central zone while the middle zone was fairly flat. The central zone was 150 times more sensitive than the limbus. This finding is very important, of course, in the fitting of contact lenses. The corneal diameter varied from 12.25 to 15.37 mms. with an average of 13.75. Many practical problems of the fitting of contact lenses are discussed. A central corneal touch produced a depression which might last for several days depending on the duration of the touch.

Paul W. Miles.

Burman, Bengt. **A simplified graphic representation of clinical findings in accommodative-convergence analysis.** Am. J. Optometry **33**:283-290, June, 1956.

In this article the author objects to the usual methods of refraction in which all patients are treated alike. When each patient receives twenty different types of examination he is regarded merely as a case or an experiment and not an individual personality. Some refraction cases should require ten minutes while others may require more than two hours. Nothing but the patient's individual problem should decide the length of the examination. Paul W. Miles.

Dinger, G. **Custom made spectacle frames with a Xantigen model.** Klin. Monatsbl. f. Augenh. **128**:607-610, 1956.

Xantigen is a clay-like material. It is warmed in water and then put on the face. A mask is obtained from this negative by pouring plaster of Paris into the negative. This will reflect all the asymmetries and pecularities of the face to which the glasses have to be fitted. (4 figures) Frederick C. Blodi.

Flamant, F. **Study of the distribution of light in the retinal image.** Arch. d'opht. **16**:54-66, 1956.

In a well-documented study from the Institute of Optics of Paris, Miss Flamant considered the distribution of light in the retinal image in patients whose pupils were larger than 0.7 mm., and for whom the laws of diffraction naturally did not apply. She notes that A. Arnulf showed in 1937 that the retinal images in eyes with pupils less than 0.7 mm. were regulated entirely by the laws of diffraction.

This basic study, documented by 10 figures and charts, will appeal to physicists and others with a special knowledge of optics, but the mathematics employed places it outside the scope of the average opthalmologist. P. Thygeson.

Gianfranco, Carlevaro. **Presentations of new optotypes for children and adults.**

Bull. et mém. Soc. franç. d'opht. **68**:199-206, May, 1955.

Demonstration of an entirely new series of visual acuity charts and their use in very young children is described. (6 figures)

Alice R. Deutsch.

Lasky, Mortimer A. **An adjustable telescopic visual aid.** Tr. Am. Acad. Ophth. **60**:216, March-April, 1956.

The aid is a monocular unit with a magnification of 2.2, mounted in a frame which has an occluder for the other eye. This device enables a patient with subnormal vision to see near or far by extending or retracting the outer end of the tube. Theodore M. Shapira.

Nordenson. **Approximation curves for sections of the anterior corneal surface.** Arch. f. Ophth. **157**:528-533, 1956.

In the central, optical segment of the cornea a symmetrical catenoid is indicated as an approximation curve for the vertical section through the ophthalmometric axis; for the horizontal section an asymmetric catenoid. For the peripheral parts of both sections a circular function serves. (1 figure, 6 tables, 5 references)

F. H. Haessler.

Popp, C. and Durchschlag, G. **Light adaptation and intraocular ischaemia.** Arch. f. Ophth. **157**:452-458, 1956.

After intraocular ischaemia for 30 seconds normal sensitivity is recovered in a few minutes but a secondary reduction of sensitivity soon occurs and lasts for hours. The acute phase is due to a blocking of the synapse, the secondary to a depression of function of the large ganglion cells of the retina. There is no reason for assuming that the process of light adaptation itself is modified by the ischaemia; it is the effect of the light stimulus on the adaptive process that is weakened in the ischemic eye. (3 figures, 11 references)

F. H. Haessler.

Savell, Arthur L. **Acuity, fixation and test projection charts and their use in the refraction room.** Am. J. Optometry **33**: 325-331, June, 1956.

In this paper, the author reviews all of the different methods of testing refraction and concludes that the projection chart is the most accurate and, also, the most convenient method to use. He emphasizes the principle that in tests for refraction the patient is most easily capable of judging whether a slight lens change has increased the acuity or not, at a threshold level of visual acuity. To reduce the visibility to a threshold level, he decreases the light intensity in the projection chart. Paul W. Miles.

Schwarz, Friedrich. **Further study of the influence of color on visual acuity.** Arch. f. Ophth. **157**:534-539, 1956.

Visual acuity was measured by means of a time-limited exposure of colored charts with Landolt rings. When the ring and the surrounding field are of the same hue the visual efficiency is best when yellow is used. When the colors of ring and chart are complementary, efficiency is best for red. Red rings in a green field are recognized with less light or shorter exposure than red rings on a red chart. The efficiency for light colored rings on a black chart is greater than for black rings on a colored chart. (3 figures, 2 tables, 7 references) F. H. Haessler.

5

DIAGNOSIS AND THERAPY

Hirschmann, Johannes. **Ocular cephalgia in diseases of extra- and intracranial organs.** Klin. Monatsbl. f. Augenh. **128**: 385-394, 1956.

This is a general survey on some problems of headache. Of special importance

to the ophthalmologist are: temporal arteritis, trigeminal neuralgia, neuralgia of the ciliary ganglion and the so-called "lower half headache" in which the sphenopalatine ganglion is affected.

Frederick C. Blodi.

Krasnov, M. **A new model of a gonioscope.** Vestnik oftal. **2**:24-28, March-April, 1956.

Krasnov describes and illustrates in detail his new model of the gonioscope. The improvement over the Goldman and Van Boiningen gonioscopes is that no solution is necessary as the tears fill up the capillary space between the gonioscope and the eye. The gonioscope is smaller so that there is more space between the gonioscope and the slitlamp, and the reflecting system can be used to greater advantage. There is also a larger surface of contact with the anterior segment of the eye and the peripheral parts of the cornea can also be examined. This is important when the central portion of the cornea is not sufficiently transparent. This gonioscope can be attached to the forehead of the patient and both hands of the examiner are free. (5 figures) Olga Sitchevska.

Lachman, R. and Lijo Pavía, J. **Ocular signs in arteriosclerosis.** Rev. oto-neuro-oftal. **30**:129-133, Sept.-Oct., 1955.

In this summary of the discussion of topics related to ophthalmology given in a round table discussion on arteriosclerosis, Lachman emphasizes the significance of early ophthalmoscopic examination in the diagnosis of arteriosclerosis. He describes the radial disposition of arterioles and venules alternatively in the macular area and points out that the first degree of arteriosclerosis consists of constricted arterioles carrying blood only to the outer limits of the macular area. Later in a second stage they even seem to retract further; because the sclerosis interferes with the flow of blood the arterioles become invisible. These two first stages are reversible.

Lijo Pavía emphasizes the importance of ophthalmodynamometry in hypertensive arteriosclerotic patients; it yields valuable prognostic signs when there is a disproportion between the diastolic pressures in the central retinal and the brachial arteries (1 figure)

Walter Mayer.

Larmande, A., Pestre, A. and Timsit, E. **Pre- and postoperative medication in uncooperative patients. (Remedial sleep and infra-curarization.)** Bull. et mém. Soc. franç. d'opht. **68**:467-479, May, 1955.

The techniques of remedial sleep and infra-curarization are described and the special indication and possible contra-indications of these treatments discussed. (1 table, 3 references) Alice R. Deutsch.

Maxwell, Euphan. **Histories of some eye conditions and their general medical background.** Brit. J. Ophth. **40**:193-215, April, 1956.

Eighty-six individual case records are briefly reviewed in a very interesting manner. The advantages of cross-indexing diseases in private files is clearly demonstrated. The cases described are outlined under the following classifications: space-occupying lesions, primary orbital tumors, diseases of the endocrine glands, diseases of the nervous system, diseases of the blood and lymphatic system, diseases of the skin, miscellaneous conditions, exogenous poisons, and psychogenic disorders. The follow-up study in most cases makes this study most pertinent and demonstrates the inter-relationship of all branches of medicine with ophthalmology. (2 references)

Lawrence L. Garner.

Pommer. **The hydrogen ion concentration during iontophoresis with buffered**

iodide solution and with natural and artificial well water products of the iodine bath of Bad Hall (upper Austria). Arch. f. Ophth. **157**:522-527, 1956.

During iontophoresis with unbuffered iodide solution, german silver cathodes, and a 0.5 mA current, there is an immediate steep rise in hydrogen ion concentration. With a 0.3 mA current the rise appears somewhat later and its course is flatter; with a carbon cathode it is irregular. With natural and artificial well water the balance of anions and cations, which act as buffer, is such that the hydrogen ion concentration is reduced to the basic side and injury to the corneal epithelium is prevented. (5 figures, 1 table, 5 references) F. H. Haessler.

Scott, Robert B. **A new type of ocular prosthesis.** A.M.A. Arch. Ophth. **55**:694-698, May, 1956.

A thin, plastic contact shell is described for fitting over blind cosmetically poor eyes. (4 figures, 1 reference)

G. S. Tyner.

Stasinska-Misiurewicz, Janina. **Use of irgapirin in some eye diseases.** Klinika Oczna **25**:129-135, 1955.

Irgapirin, which is a mixture of aminopirin and the sodium salt of butazolidin, was given by intramuscular injection to 16 patients of whom 10 had uveitis, two scleritis, two trigeminal neuralgia and two fresh macular exudates. Photophobia, lacrimation, hyperemia of the iris and the headaches were improved. Corneal precipitates were promptly absorbed. Irgapirin was most effective in acute conditions; chronic uveitis and vitreous opacities were not affected by its use. Treatment with irgapirin should be continued beyond the apparent cure to prevent recurrence. There is a certain similarity of irgapirin to cortisone, without, however, the unpleasant side effects. Eight case histories are presented. (13 references) Sylvan Brandon.

Velhagen, Karl. **Ophthalmologic experience with Perlon.** Arch. f. Ophth. **157**:429-451, 1956.

Velhagen has used Perlon, a synthetic plastic, as material for sutures exclusively since 1950. He very rarely uses silk, and catgut only when he desires rapid absorption. He also uses bands, nets, "cotton," and orbital implants made of Perlon. He reports his clinical experience as well as histologic and experimental investigation of this material which he found satisfactory. (18 figures, 57 references) F. H. Haessler.

Zanen, J. **Requirements for the detection and correct interpretation of central color scotomas.** Bull. et mém. Soc. franç. d'opht. **68**:188-195, May, 1955.

The tracing of central color scotomas has been generally neglected in spite of its possible diagnostic value, probably because of the roughness and lack of thoroughness in the methods available. The scotometer demonstrated by the author and manufactured by Haag-Streit of Bern represents the results of many years of extensive research. The enormous difficulties in building a similar instrument could only be achieved by expert knowledge of every physiological fact. The new scotometer utilizes spectral colors and permits regulation in the intensity of stimulus and adjustment in size in the exposed area. The pupils should remain unchanged. The fixation always is central. The time of exposure can be reduced to 1/2000 of a second. The intensity of illumination is measurable by a photopile of Gossen. The electronic photovolt model 512M of the Photovolt Corporation has proved equally useful but deviated towards the violet end of the curve. The interferential filters can be

modified as indicated. (3 figures, 2 tables)
Alice R. Deutsch.

6
OCULAR MOTILITY

Dupuy-Dutemps, P., Paquet and Vergue, J. L. **Classification of diplopia after squint operations.** Bull. et mém. Soc. franç. d'opht. **68**:159-174, May, 1955.

Diplopias immediately after strabismus operations have a good prognosis as they are time limited. The diplopias which persist longer than three weeks present a more serious problem. The causes for the latter type of diplopia in cases of concomitant convergent squint were investigated. Two main groups were recognized: 1. the diplopias of extrinsic origin included manifest over-correction, minimal over-correction, involuntary convergence and variances between adduction and abduction, and 2. the diplopias of intrinsic origin occurred with pronounced negative or positive angle β, in abnormal retinal correspondence and in cases of anisometropias and amblyopias. The latter were often not easy to detect or to explain. They also were less consistent and often could be overcome by training. Related phenomena like suppression, superposition of images instead of fusion of images and newer methods of examination are discussed at length. Those of group 1 were thought to be obstinate and difficult to handle. They often needed repeated surgery. Alice R. Deutsch.

Friede, Reinhard. **Surgical treatment of severe nystagmus.** Klin. Monatsbl. f. Augenh. **128**:451-455, 1956.

In cases of severe, coarse nystagmus the author disinserts the horizontal rectus muscles and sutures them to the orbital periosteum. If the nystagmus is rotatory the inferior rectus muscle must be cut also. This method gave good results in three patients. When operating for congenital cataract the author prefers the suction method. Frederick C. Blodi.

Girard, Louis J. **Pseudoparalysis of the inferior oblique muscle.** South. M. J. **49**:342-346, April, 1956.

Pseudoparalysis of the inferior oblique muscle is a term suggested when the underaction is secondary to structural changes in the superior oblique tendon or its sheaths, which may be congenital or postoperative, or to anomalous check ligaments on the inferior oblique insertion. Four types are described: 1. congenital retraction of the tendon sheath of the ipsolateral superior oblique muscle; 2. postoperative retraction of the tendon sheath of the superior oblique; 3. anomalous check ligaments on the inferior oblique; and 4. swelling on the superior oblique tendon passing through the trochlea. The diagnosis is made at the time of surgery. (8 figures, 1 reference)
Irwin E. Gaynon.

Jonkers, G. H. **The results of orthoptics and of surgery.** Bull. et mém. Soc. franc. d'opht. **68**:497-506, May, 1955.

The author reviews 137 cases of strabismus. In convergent squint a complete cure, namely normal binocular vision, was established in 35.8 percent with orthoptic exercise alone or with orthoptic therapy and surgery. There were eight cases of accommodative convergent squint with 75 percent cure on orthoptics, only. In 42 cases convergent squint with normal correspondence was achieved in 50 percent. In this group only seven cases were without surgery. Of the 65 patients with abnormal correspondence 12.3 percent were made normal. Three patients were operated on before orthoptics were started and three during orthoptic training. Two patients had no surgery. Among the 22 patients with divergent strabismus 63 percent were cured, four with and four without surgery. Alice R. Deutsch.

Riehm, G. **Unusual ocular findings in myasthenia gravis.** Klin. Monatsbl. f. Augenh. **128**:613-615, 1956.

A 39-year-old woman with myasthenia experienced a sudden bilateral ophthalmoplegia. The ocular motility could not be influenced by any of the cholinesterase-binding drugs. (20 references)

Frederick C. Blodi.

Urist, Martin J. **The surgical treatment of esotropia with bilateral depression in adduction.** A.M.A. Arch. Ophth. **55**:643-665, May, 1956.

The author suggests resection of one or both lateral rectus muscles for low degrees of esotropia, mostly present on upward gaze. (9 figures, 7 tables, 2 references)

G. S. Tyner.

7

CONJUNCTIVA, CORNEA, SCLERA

Barraquer-Moner, Joaquin. **Keratoplasty. Personal results.** Bull. et mém. Soc. franç. d'opht. **68**:414-449, May, 1955.

Seventy cases of keratoplasty as performed by the author in 1954 are reviewed. Satisfactory results were achieved in 85.1 percent. Sixty-one case histories are discussed. Details of the preliminary examinations and treatments, particularly in the surgical techniques, in the instruments and in postsurgical care, are described. The late clouding of the graft without local complications, like anterior synechias, displacement of the graft or hypertension is considered to be one of the most unfortunate situations. It is ascribed to a local tissue hypersensitivity, not to focal infection or traumatic injury of too many sutures. Early replacement of the cloudy graft by another graft is considered to be the treatment of choice. (2 tables, 24 figures, 14 references)

Alice R. Deutsch.

Bietti, G. B., Guerra, P. and Ferraris de Gaspari, P. F. **The band-shaped, nodular dystrophy of barren, tropical lands. A clinical, anatomical and pathological study.** Bull. et mém. Soc. franç. d'opht. **68**:101-129, May, 1955.

The bandshaped, corneal dystrophy of barren lands has been described previously but a detailed etiologic and clinicopathologic study of this disease was never made. It represents a definite clinical entity, restricted to the regions of Eritrea, the islands of the Red Sea and the Persian Gulf, to Italian Somaliland and to Saudi Arabia, possibly also to countries of similar climatic conditions. Etiologic factors are probably rapid evaporation, increased concentration of tears, microtrauma and chemical irritation due to contamination of the atmosphere. The preponderance of affected males is ascribed to the difference in habits and costoms of males and females among the Mohammedan population. The clinical picture consists of an initial very delicate superficial cloudiness in the inferior third of the cornea, mostly temporal to the vertical meridian. The opacity increases in density, takes a nodular appearance and enlarges especially in the horizontal direction. Its color changes from grayish to yellowish. It never reaches the corneal periphery. Inflammatory signs are entirely absent. The beautiful pathologic slides show the lesions to consist of hyalin deposits first in the region of Bowman's zone, later on also in the epithelium and superficial parenchyma. During the course of the disease a patchy disappearance of Bowman's membrane and a thickening and keratinization of the epithelium were noted. There was also a breakdown of the superficial corneal lamellae. Deposits of calcium coagula were visible. Some eyes had trachoma simultaneously; however, trachoma was not thought to be of importance in the etiology of this disease, neither were the physical nor nutritional status of the patient considered to be contributory.

The hereditary corneal dystrophies of Groenov, the nodular dystrophy of Salzman and the classical band-shaped keratopathy were found to have a general likeness to this disease. The dissimilar features of each entity were described in detail.

Sixty-nine patients were observed by the authors. Forty-six were natives of Eritrea, twenty-three were from Saudi Arabia. The findings concerning those patients were presented in tables. The only effective treatment was lamellar keratectomy, which because of the superficial location of the lesions presented a clear remaining cornea. Unfortunately this improvement often was only temporary. (12 figures. 2 tables, 8 references)

Alice R. Deutsch.

Bonnet, P. **Band-shaped opacity of the cornea. (A critical review.)** Arch. d'opht. **16**:12-43, 1956.

In a critical review of this corneal dystrophy, Bonnet concludes that its occurrence in an otherwise healthy eye is an indication for an intensive ocular and systemic study. He considers that the primary form has greatest interest but is least understood, and that cases secondary to iridocyclitis are most frequent and best understood. In the infant the opacity is a manifestation of chronic rheumatism, usually Still's disease. It as a part of the characteristic triad: torpid iridocyclitis, band-shaped opacity, and eventual cataract. The finding of the opacity in an infant without arthritis is considered an almost certain indication of approaching rheumatism. A few exceptions have been noted. In the infant cerebrospinal meningitis with uveal involvement, and occasionally toxoplasmosis, may result in band-shaped opacity.

The author discusses in detail the pathologic anatomy of the condition and its various clinical forms. He further discusses treatment in its different aspects, particularly the various chemical methods of removing the calcium deposits. He contrasts the chemical methods with lamellar keratoplasty and concludes that perforating keratoplasty is rarely if ever indicated. He stresses that in early cases treatment of the underlying uveitis or glaucoma is essential. P. Thygeson.

Cavka, V. **Sclero-corneal-conjunctival transplant in total symblepharon.** Bull. et mém. Soc. franç. d'opht. **68**:140-141, May, 1955.

In extensive ankylosymblepharon and severe recurrent pterygium with shrinkage of the fornices it is impossible to excise a sufficient amount of mucous membrane to replace the defects in the conjunctiva of the lids or bulbi. Mucous membrane grafts from other parts of the body, like the vagina or penis or Thiersch flaps, gave poor functional and cosmetic results. In the method described a corneo-sclero-conjunctival graft, taken from a cadaver, is transplanted after separation of the adhesions. Sutures were placed through the sclera at the limbus and through the conjunctiva at the margins of the graft. A contact glass was inserted and the antibiotics of choice were applied. The corneal part of the graft always becomes integrated. It has to be removed about one month after operation. In the ten patients operated on the graft had taken in this period. There was more or less violent local reaction but definite improvement in the appearance of the eyes. (8 figures, 8 references)

Alice R. Deutsch.

Coyle, E. F. **Scleroderma of the cornea.** Brit. J. Ophth. **40**:239-241, April, 1956.

This is probably the first recorded case of scleroderma of the cornea. A single patient is described who had scleroderma of the forehead with gradual extension onto the cornea. Since the corneal epithelium is ectodermal, it was assumed that

the lesion was scleroderma. No biopsy was done. (3 references)

Lawrence L. Garner.

Friemann, W. and Overhoff, W. **Keratitis as an occupational hazard for men working with oily herrings.** Klin. Monatsbl. f. Augenh. **128**:425-438, 1956.

These herrings are caught because of their oil content and when unloading them oily fluids are often splashed into the eyes of the workers. Frequently a conjunctivitis develops which may lead to a superficial keratitis. In two patients extensive corneal scars remained.

In some animal experiments similar lesions could be produced in rabbits with the application of some ptomaines (neurin, cholin and methylamine). Early application of a cortisone ointment is the treatment of choice. (6 figures)

Frederick C. Blodi.

Guimaraes, Wilson. **Dermoid, lipoma and dermolipoma of the conjunctiva.** Rev. brasil. oftal. **15**:55-61, March, 1956.

The author reviews briefly the general characteristics of these three types of tumors and presents a pathologically proven case of each one of them. In his case of lipoma, diplopia developed after surgery which the author attributes to the limitation of ocular motion caused by an adhesion between the conjunctiva and the globe. He advises that Tenon's capsule be placed between these two structures at the end of the operation in order to prevent this complication. (5 figures, 9 references) Walter Mayer.

Jurin, P. **Intracellular inclusions in vernal catarrh.** Vestnik oftal. **2**:9-11, March-April, 1956.

Intracellular inclusions in vernal catarrh are stained violet by a 1 percent aqueous solution of methylene blue in three to five minutes. In contrast to Prowazek's bodies, the inclusions in vernal catarrh are situated around the nucleus of the epithelial cell and have no caps, which are characteristic for the Provazec's bodies. Many intracellular inclusions were found in 49 patients, 22 of whom came to the laboratory with a diagnosis of trachoma. In the majority of these patients there was also eosinophilia. Many inclusions were always found in advanced vernal catarrh. Jurin believes that these inclusions are specific formations of virus origin.

Olga Sitchevska.

Marconcini, Eraldo. **A case of spinocellular epithelioma of the bulbar conjunctiva following a recurrence of a pterygium.** Arch. di ottal. **60**:66-73, Jan.-Feb., 1956.

A patient who had been operated upon twice for a pterygium on the temporal side, developed a spinocellular epithelioma of the conjunctiva in the same location. (2 figures, 17 references)

John J. Stern.

Rais. **Keratoplasty in corneal staphyloma.** Bull. et mém. Soc. franç. d'opht. **68**:410-414, May, 1955.

A perforating keratoplasty was performed in one case of partial and two of total corneal staphyloma. Iris and cornea were resected in one block and the 9 mm.-wide defect was replaced by a corneal graft, using direct sutures. The local irritation was comparatively small, the formerly increased ocular tension became normal and the cosmetic result was very satisfactory. Originally this operation was devised for reconstructive reasons only. The surprising recovery of the shape of the eyeball, the absence of severe inflammatory reactions and the normalization of the ocular tension were very encouraging and it was hoped that in some of these otherwise hopeless cases the "tectonic" keratoplasty may be followed by an optic keratoplasty. (1 figures)

Alice R. Deutsch.

Sommer, Gerd. **Corneal changes in congenital aniridia.** Klin. Monatsbl. f. Augenh. **128**:459-466, 1956.

In two families with aniridia a progressive corneal degeneration was observed. The opacities are first crescent-shaped in the periphery but may advance and cover the entire limbus. Vascularization follows. The entire cornea may become affected. (5 figures, 13 references)

Frederick C. Blodi.

Speakman, J. S. and Jones, J. D. **Corneal trephining for penetrating keratoplasty.** Brit. J. Ophth. **40**:216-221, April, 1956.

To facilitate better results in keratoplasty a new device is described which assures better apposition of the graft. Rabbit and monkey eyes were employed with a special holding instrument which permits immobilization of the eye as well as control of the intraocular pressure of both the donor and recipient eye. The shape of the graft can thereby be maintained to a uniform degree, since in using a manual trephine the bevel of the graft is affected by the intraocular pressure. By using the above technique one can with some experience obtain a corneal disc which has a constant bevel, thus fits the recipient eye better. (9 figures, 12 references) Lawrence L. Garner.

Sysoyev, F. **Prowazek's bodies in trachoma and their epidemiologic significance.** Vestnik. oftal. **2**:3-9, March-April, 1956.

Scrapings from the conjunctiva of 2,933 subjects were examined for the presence of Prowazek's bodies; 491 had trachoma stage III, 795 had trachoma stage IV, 265 had conjunctivitis, and 1,297 had clinically healthy eyes. This study was undertaken with the purpose of establishing whether there are carriers of the Prowazek bodies in healthy or clinically-cured trachomatous eyes. In trachoma stage IV foci of trachoma and deeply situated follicles were observed. Prowazek's bodies were found in so-called cured trachoma, which has an epidemiologic significance. There was a possibility of "carrying" trachoma in healthy eyes. Patients with latent or microtrachoma are virus carriers; under certain conditions the characteristic picture of trachoma may flare up. The criterion of a cured trachoma with no danger of recurrence is not fully established; therefore, there should be constant observation of the cases of trachoma, stage IV and the period of observation should be extended as long as necessary. Olga Sitchevska.

Trantas, Nico G. **A special type of keratopathy, caused by local dehydration.** Bull. et mém. Soc. franç. d'opht. **68**:401-409, May, 1955.

The keratopathy described occurs predominantly in the paralimbic area close to the 3 to 9 o'clock meridian. About 1/3 to 3/4 of the corneal thickness is involved. The lesion is about 1.5 mm. in size, has a dry surface and sharp, semitransparent margins. During a slitlamp examination the lesion may increase in size and depth and it disappeared temporarily whenever water was dropped on the cornea or a bandage applied. Four different types of these lesions were recognized, dependant on their size, depth, location and other simultaneously existing ocular abnormalities. They were observed in the presence of pterygium, subconjunctival hemorrhage, after squint operations, subluxated lenses and iridocyclitis. The ephemeral appearance and disappearance of this dehydration phenomenon was ascribed to an angioneurotic origin, to disturbances in the composition and formation of the precorneal film and possibly to circulatory changes in the limbal circulation. (5 figures)

Alice R. Deutsch.

Urrets-Zavalia, Jr., Alberto. **Removal of calcific corneal deposits with EDTA.** Arch. oftal. Buenos Aires **31**:64-66, Feb., 1956.

Removal of calcific corneal opacities may be performed successfully by means of repeated instillation of a 0.01 M aqueous solution of disodium ethylendiamine tetraacetate dihydrate (EDTA). The affected areas must be previously denudated of the overlying epithelium. In a treated case of band-shaped corneal degeneration secondary to a long-standing "granulomatous" iridocyclitis of a probably tuberculous origin, the superficial corneal opacity cleared completely, only to reappear almost completely after a seven-months interval. Although the case here reported confirms the ability of the drug to remove calcific deposits in band-shaped keratopathy, it also shows that recurrences in the form of similar deposits are apt to occur since the underlying, fundamental dystrophic condition remains unmodified. Accordingly, it is thought that EDTA may be more useful in cases of calcific deposits of an exogenous and accidental nature than in those where they result mainly from an organic disturbance. (7 references) A. Urrets-Zavalia, Jr.

Weekers, L. **The role of dormant virus in the pathogenesis of certain keratitides.** Arch. d'opht. **15**:839-845, 1955.

The author discusses the role of dormant viruses, particularly herpes simplex virus, in the production of keratitis, and cites a number of cases of dendritic keratitis which followed minor corneal injuries. He reviews the literature relating to the role of industrial or other trauma in awakening dormant herpes simplex virus, and discusses the medicolegal significance of this relationship. He then discusses the nature and various causes of superficial punctate keratitis, with special reference to the role of viruses. He concludes with a discussion of the various stimuli that have been known to reactivate dormant viruses, again with special reference to herpes simplex virus.

P. Thygeson.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Busacca, Archimède. **Biomicroscopy of the normal and diseased ciliary body.** Bull. et mém. Soc. franç. d'opht. **68**:297-305, May, 1955.

The findings in a biomicroscopic study of the posterior chamber of the living eye are compared with findings in pathologic specimens. An anterior hyaloid membrane with adherence of a layer of vitreous was seen in normal eyes. The positions of Hannover's, Petit's and Berger's spaces in various stages of zonular activity are described and also an additional circular membrane behind the posterior zonular fibers, the so-called plicata of Vogt. This latter membrane delimits a space corresponding with the most anterior part of Cloquet's canal; some authors considered this band to be fibrous, connecting the vitreous to the pars plana of the ciliary body; others believed it to be just a part of the hyaloid membrane. Not only the perilenticular spaces but also the anterior and posterior parts of the ciliary body were investigated. Those parts were scrutinized up to the ora serrata. Koeppe's contact lenses were used for the examinations. The pupils were widely dilated. Several eyes had had iridectomy. Others were aphakic after extra- or intra-capsular cataract extraction. With the techniques described, extraordinary and interesting structures were revealed, belonging to a region otherwise difficult to inspect. (6 figures) Alice R. Deutsch.

Christensen, L., Swan, K. C. and Huggins, H. D. **The histopathology of iris pigment changes induced by miotics.**

A.M.A. Arch. Ophth. **55**:666-671, May, 1956.

The nodules or cysts which form in the area of the iris sphincter after prolonged use of a miotic, disappear after cessation of the therapy. Histologic sections of an eye with these changes disclosed that the "cysts" are actually solid accumulations of pigmented epithelial cells. There is also proliferation of the iris pigment epithelium beyond its normal limits. The presence of such nodules in an aniridic eye probably disproves the idea that they are caused by excessive stimulation of the sphincter. (9 figures, 5 references)

G. S. Tyner.

Donovan, Bernard F. **Neurilemona of the ciliary body.** A.M.A. Arch. Ophth. **55**:672-675, May, 1956.

An example of the rare intraocular occurrence of this tumor is reported. The tumor appeared as a cystic or solid mass seen in the inferior temporal quadrant of the fundus. In the course of four years the tumor became enlarged and produced bulging of the ciliary body and iris. The eye became inflamed and glaucomatous and had to be enucleated. Histologic examination revealed benign nature of the tumor. (3 figures, 8 references)

G. S. Tyner.

Gerewitz, H. **Iris cysts in normal eyes.** Klin. Monatsbl. f. Augenh. **128**:610-613, 1956.

These cysts were observed on both eyes of a healthy 19-year-old man who had never received any miotic drugs. (4 figures)

Frederick C. Blodi.

Huszcza, Alfred. **Complement titer before and after the use of typhoid vaccine in focal eye diseases.** Klinika Oczna **25**:113-122, 1955.

The author describes modern concepts of the structure of the complement and of its function in the human body. The method of the measuring of the complement is described. It was found that in 23 patients with uveitis the complement level increased 44 percent in comparison with patients without focal infection; the injection of typhoid vaccine brought the complement level to normal in proportion to the improvement in the clinical condition. (4 tables, 55 references)

Sylvan Brandon.

Liegl, Otmar. **Drusen of the fundus in pseudoxanthoma elasticum.** Klin. Monatsbl. f. Augenh. **128**:467-473, 1956.

A 12-year-old girl with numerous drusen of Bruch's membrane in both eyes was observed. No angioid streaks were present. (3 figures, 57 references)

Frederick C. Blodi.

Sédan, J., and Guillot, P. **Uveitis medicamentosa.** Bull. et mém. Soc. franç. d'opht. **68**:317-323, May, 1955.

The authors review the case histories of four patients with severe uveitis which followed a therapeutic procedure which was the injection of tetanus antitoxin in a sensitized individual in one case and of Friedman's serum in a patient with healed pulmonary tuberculosis in another. In a third case the uveitis occurred after an implanation of placenta after extraction of cataract. The fourth patient had a still active tuberculosis when the cataractous lens was extracted from his only eye. He developed severe uveitis, possibly as a result of sensitization by massive resorption of necrotic material from the lungs during treatment with streptomycin. In this latter case, however, the allergic etiology could not be proved. This study establishes drug allergy as a possible cause of uveitis. It is always important to differentiate allergy and hypersensitivity from drug intolerance, which is the manifestation of irritation and intoxication by a dose which is considered normal and safe.

Alice R. Deutsch.

Stankovic, Ivan. **Etiology of the iridocyclitis following Papatacci fever.** Bull. et mém. Soc. franç. d'opht. **68**:307-316, May, 1955.

During the last two years many cases of Papatacci fever were observed in different regions of Yugoslavia. Some cases were followed by a bilateral diffuse serofibrinous iridocyclitis which subsided slowly and completely. The anterior segment usually cleared faster than the posterior. The most severe complication observed was a papillitis in a six-year-old child. The ocular tension was always found to be normal. The treatment consisted of the instillation of atropine, hot packs, cortisone and a variety of antibiotics, salycilates and foreign proteins. The systemic treatment seemed not to have too much effect on the cause of the disease. The importance of a detailed clinical history, of complete physical examination and possible detection of the cause in every case of iridocyclitis was stressed. Papatacci fever is caused by a filtrable virus and is transmitted by mosquitoes. It has been the subject of several papers; a concomitant iridocyclitis apparently was not noted before. (15 references) Alice R. Deutsch.

Wilczek, M. and Feltynowski, A. **Investigation of sympathetic ophthalmia with electron microscope.** Klinika Oczna **25**:77-79, 1955.

The eye was enucleated three months after a perforating injury in the area of the ciliary body. The other eye showed symptoms of sympathetic ophthalmia but recovered under treatment with chloromycetin and streptomycin. The uvea from the enucleated eye was prepared according to Cox. Virus bodies were discovered with the electron microscope. There were small oval bodies 60 millimicrons and large composite particles of 100 to 160 millimicrons in size. Further investigation is necessary to determine whether these virus bodies are the cause of sympathetic ophthalmia. (2 figures, 4 references)

Sylvan Brandon.

9

GLAUCOMA AND OCULAR TENSION

Arruga, H. and Arruga, A. **Diamox in ocular hypertension.** Bull. et mém. Soc. franç. d'opht. **68**:175-187, May, 1955.

The importance of Diamox in the treatment of ocular hypertension is recognized. Its action, however, is thought to be only temporary. The most conspicuous results were achieved with acute glaucoma, glaucoma secondary to uveitis, surgery and trauma. It was found to be useful in presurgical care before intra-ocular surgery, for example, lamellar keratoplasty, or surgery for iris prolapse and subluxated lens. The operations should preferably be performed during the time of maximum action of the drug. Diamox also reduces the edema of the retina after detachment operations and lowers the hypertension after diathermy coagulation. It depresses the tension in a glaucomatocyclitic crisis when other medication has failed. Eyes with chronic glaucoma with fair miotic control were improved by Diamox. It was beneficial whenever the pupils of hypertensive eyes had to be dilated. Eyes with far advanced absolute glaucoma were not benefited but a certain amount of reduction of tension could be observed in recent cases.

Diamox was used in 74 persons, 58 of whom had increased tension and the effectiveness of Diamox in a variety of eye diseases is acknowledged. Its use however should be limited to short periods, especially in patients with kidney and heart diseases. (15 references)

Alice R. Deutsch.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 12th of the month. For adequate publicity, notices of postgraduate courses and meetings should be received three months in advance.

Deaths

Dr. Lucian Orville Clement, Salem, Oregon, died April 26, 1956, aged 80 years.

Dr. William Franklin Hughes, Indianapolis, Indiana, died April 21, 1956, aged 83 years.

Yale clinical conferences

Yale University School of Medicine, New Haven, Connecticut, announces a series of teaching conferences planned especially for ophthalmologists and conducted by the Section of Ophthalmology, Dr. Rocko M. Fasanella, chairman. The conferences, which are usually held on alternate Fridays, begin on November 9, 1956, and continue through March 29, 1957. The hours are from 3:45 to 5:00 p.m. The fee for the series is $15.00.

The following discussions have been scheduled for the conferences:

November 9th: "Psychologic considerations in surgery," Irving Janis, Ph.D., associate professor of psychology, Yale University. Comments by Theodore Lidz, M.D., professor of psychiatry, and Edith Jackson, M.D., clinical professor of pediatrics and psychiatry, Yale University School of Medicine.

November 16th: "Reoperations and the management of complications in glaucoma surgery," Edmund B. Spaeth, M.D., Philadelphia.

December 14th: "Lids and facial burns: Newer concepts of management," Donald P. Shedd, M.D., assistant professor of surgery, Yale University School of Medicine.

January 11, 1957: "Surgery in congenital glaucoma," Harold G. Scheie, M.D., Philadelphia.

January 25th: "Keratoplasty: Reoperations and management of complications," R. Townley Paton, M.D., New York.

February 8th: "Eye pathology: Some unusual cases," David Freeman, M.D., Yale University School of Medicine.

February 22nd: "Vitreous transplants," Donald M. Shafer, M.D., New York.

March 8th: Film "Embryologic development of the eye." Discussion by Leon S. Stone, Ph.D., Yale University School of Medicine.

March 29th: "Medical management of surgical complications," Irving H. Leopold, M.D., Philadelphia.

Course on glaucoma

A seminar on glaucoma with particular emphasis on gonioscopy and the study of the anterior angle will be given at the Brooklyn Eye and Ear Hospital on November 12, 13, and 14, 1956. Ample opportunity for practical instruction in the use of the gonioprism will be given and material from the glaucoma clinic will be utilized.

The course will be given by Dr. Daniel Kravitz, assisted by Dr. Mortimer A. Lasky, Dr. Arthur Shainhouse, Dr. A. Benedict Rizzuti, and Dr. Abner S. Rosenberg. Registration is limited to six ophthalmologists only.

Application and the fee of $50.00 may be addressed to:

Dr. Daniel Kravitz
Brooklyn Eye and Ear Hospital
29 Greene Avenue
Brooklyn 38, New York.

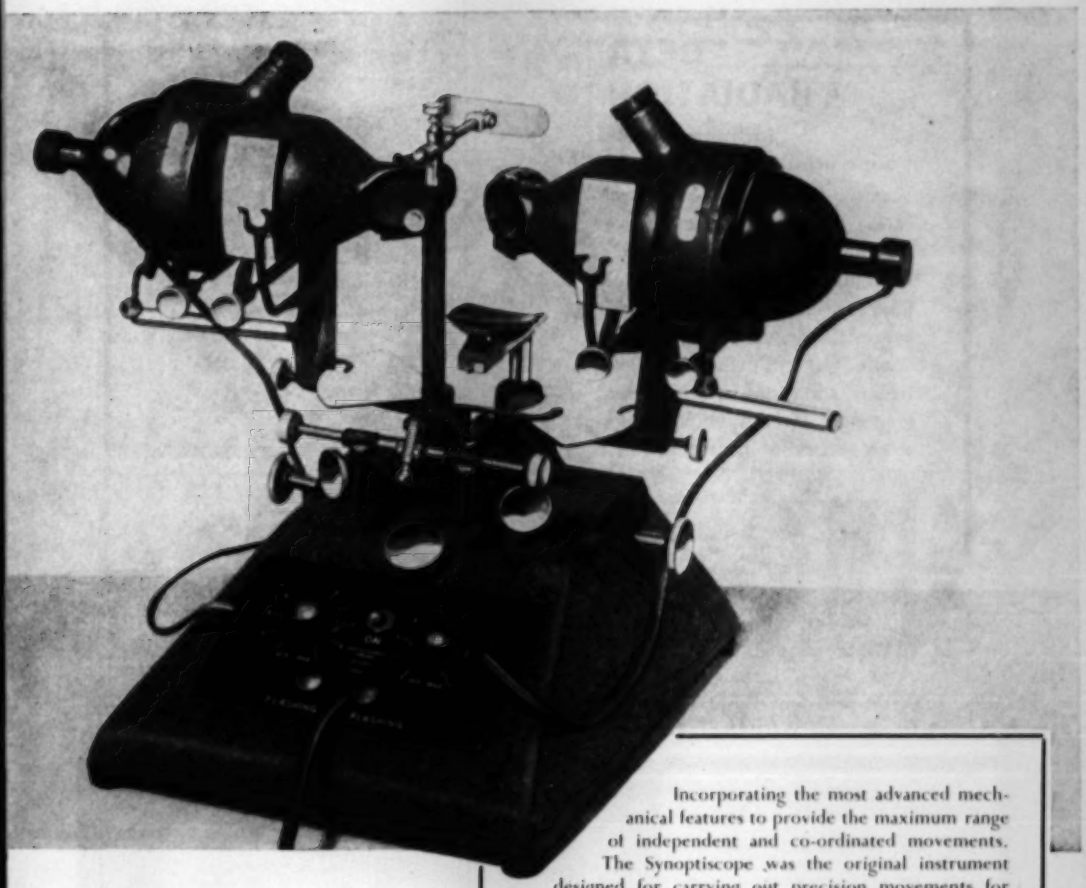
Basic course

A basic course in ophthalmology will be made available to graduates of approved medical schools through the University of California Extension on Wednesdays from 7:00 to 9:00 P.M. next September 26, 1956, through May 29, 1957.

Sessions will be held in the Old Religious Conference Building, on the Los Angeles campus of the university.

The course has been planned to assist candidates in preparing for the American Board of Ophthalmology examinations, and will offer a study of the basic subjects in ophthalmology as outlined in the syllabus prepared by the American Board of Ophthalmology, namely: physiological optics and refraction, embryology, histology, anatomy, chemistry, physiology, neurologic ophthalmology, perimetry and pharmacology. This course is made possible through a grant from the Spratt Optical Company and the Superior Optical Company. Scholarships are available without charge to all qualified eye residents who wish to take the course.

Application forms for enrollment and detailed copies of class information are available on request to Medical Extension, University Extension, University of California, Los Angeles 24, California.



THE SYNOPTISCOPE by CURRY & PAXTON

INCORPORATED

230 PARK AVENUE · NEW YORK 17, N.Y.

Manufacturer's Representatives in the U.S.A.

Service & Assembly Plant:
866 Willis Avenue, Albertson, Long Island, N.Y.
Complete service, repair and parts department

Incorporating the most advanced mechanical features to provide the maximum range of independent and co-ordinated movements. The Synoptiscope was the original instrument designed for carrying out precision movements for Orthoptic training.

MAIN FEATURES

1 **New wide field** eye pieces and larger mirrors, brighter illumination with high intensity gas filled bulbs. 2. **Accurate measurement** of horizontal ductions, vertical ductions and cyclo ductions under the stimulus of Stereoscopic vision or otherwise. 3. **Precise, controlled and unrestricted** exercise of the external ocular motor muscles. *(This function is of especial value where the correcting lenses are not readily accepted by the patient, or where it is required to build up a duction reserve).* 4. **Relaxation exercises.** 5. **Treatment of squint,** including: development of simultaneous macular preception; development of fusion; development of stereoscopic vision and fusional reserve; co-ordination of hand and eye; co-ordinating eye movements.

SUPPLEMENTARY FEATURE
Streak slides for the Bielschowsky after image test.

Other Ophthalmic Instruments manufactured by Curry & Paxton of England include:

SLIT LAMPS · OPHTHALMOSCOPES · THE FOVEOSCOPE · STREAK RETINOSCOPES · MADDOX WING TEST · MADDOX HAND FRAME DIPLOSCOPE · CHEIROSCOPE · TRIAL FRAMES · TRIAL CASES ORTHOPTIC APPARATUS

DISTRIBUTORS: *Chicago:* House of Vision *San Francisco:* Parsons Laboratories *Pittsburgh:* Doig Optical

BETA RADIATION

for treatment of superficial corneal diseases

You will be interested in the scientific data compiled in our booklet, "Radiation Therapy Sources." It includes clinical data, indications for treatment by irradiation, suggested dosage table, U. S. Atomic Energy Commission regulations, and a description of our improved M-1 Applicator. It's yours without obligation.

The M-1 Strontium-90 Applicator

Armamentarium

V. MUELLER & CO.

330 South Honore Street
Chicago 12, Illinois
Rochester, Minn. • Dallas, Tex. • Houston, Tex.

Instruments of ophthalmology: *Costenbader Accommodometer*

Determining acuity, convergence, and punctum proximum of accommodation are done efficiently with the Accommodometer. Held in one hand, it presents a variety of easily changeable symbols at close distances measured from the outer orbital rim. Acuity at one-third meter is determined by symbols graduated from 20/400 to 20/20.

ACCOMMODATIVE ESOTROPIA diagnosis and treatment finds the Accommodometer valuable for determining accurately the least hyperopic correction which will maintain good vision and good binocular alignment. Various techniques are described in literature we will be happy to send you.

Developmental laboratories, prescription services, the West's most complete surgical and diagnostic showroom

Write: Dept. 7, 518 Powell St. San Francisco, California

Parsons Optical LABORATORIES

PRESCRIPTION OPTICIANS

ST. LOUIS, MO.

Erker Bros. Optical Co.

908 Olive Street
518 N. Grand Boulevard
and 33 N. Central Ave., Clayton, Mo.
Prescription Opticians Since 1879

CHICAGO, ILL.

ALMER COE & COMPANY

Prescription Opticians
Established 1886
10 N. Michigan Ave.
1645 Orrington Ave., Evanston, Ill.

Dow Optical Co.

PRESCRIPTION SPECIALISTS

Suite 1015 30 N. Michigan Avenue
Chicago, Illinois
Phone RAndolph 6-2243-44

DEALERS IN OPHTHALMOLOGICAL EQUIPMENT

PORTLAND, ORE.

Hal. H. Moor, 315 Mayer Bldg.

Guild Optician

Oculists' prescriptions exclusively

"OPHTHALMIC LITERATURE"

AN ABSTRACT JOURNAL IN ENGLISH OF THE WORLD'S CURRENT LITERATURE ON OPHTHALMIC SUBJECTS

Indispensable to the busy practitioner for quick reference and timely useful information.

"Ophthalmic Literature" and Index (8 numbers) Yearly subscription—Four Guineas ($13.50 U.S.A.). Published by British Medical Association.

U.S.A. Agent

GRUNE & STRATTON, INC.
381 Fourth Ave.
New York 16, New York

CINCINNATI, OHIO

L. M. Prince Co.

Established 1872

Prescription Opticians

Sole makers of Coflexic

Corrected Curve Lenses

E. B. Meyrowitz

SURGICAL INSTRUMENTS CO., INC.
520 FIFTH AVENUE, NEW YORK 36, N. Y.

LONDON ***ESTABLISHED 1875*** **PARIS**

THE CHAMLIN PERIMETER

Dr. Max Chamlin, New York City

This single instrument takes the place of a perimeter, the supporting ophthalmic table, and a chin rest for tangent screen study.

Arc swings out of way to right or left on vertical axis for tangent screen use.

Has fixed light source under chin rest in median position, which affords exactly equal illumination nasally and temporally in all 360° of rotation.

A metal guard prevents entanglement with patient's clothes as arc swings through 270° meridian.

A small crank raises or lowers perimeter. The height is not affected by weight of the patient's head. Supplied with test objects and record charts.

With Test Objects—$350.00 (F.O.B.—N.Y.C.)

See Us at the A.A.O.O. Convention—Palmer House, Chicago, Ill., Oct. 14-19, Booths 79 & 80

No. B-14

BERENS PRISM BARS

are the accepted instrument for the rapid performance of the screen test, for measuring all forms of muscular unbalance and for prism exercise.

VERTICAL
17 x 30mm. prisms
No. B10
½-1-1½-2-3-4-5-6-8-10
Price $16.50

No. B14 1-2-3-4-5-6-8-10-12-14-16-18-20-25
Price $27.50

HORIZONTAL
17 x 30mm. prisms
No. B5 3-5-10-15-20
Price $11.00

No. B5R 3-5-10-15-20 Red
Price $12.00

No. B6 1-3-5-10-15-20
Price $12.50

No. B15 1-2-4-6-8-10-12-14-16-18-20-25-30-35-40
Price $27.50

Large bars with 28 x 30mm. prisms

No. LB14 1-2-3-4-5-6-8-10-12-14-16-18-20-25
Price $35.00

No. LB15 1-2-4-6-8-10-12-14-16-18-20-25-30-35-40
Price $35.00

Available at all optical and surgical suppliers

Manufactured by

No. B-15

4920 N. Lawrence Street R. O. GULDEN Philadelphia 20, Pa.

Our new complete brochure is now available

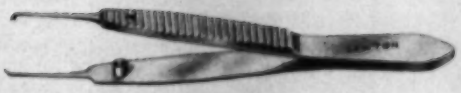
LAWTON

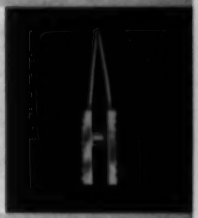
Corneoscleral Suture Forceps by John J. Sauer, M. D.

This new suture forceps has been designed to afford firm fixation of the cornea or sclera with a minimum amount of tissue trauma.

The over-all length of the instrument is 70 mm. The shaft is 13 mm long and 1.0 mm wide. The forceps has 1x2 angular teeth, which are 0.6 mm long and very strong. A stop prevents excessive overlapping of the teeth, thereby limiting the bite into the tissue. The forceps will not hold the conjunctiva, the latter sliding free between the teeth. Stainless Steel $7.00 each.

Available Only Through Authorized Surgical Supply Dealers.





THE Lawton COMPANY • 425 FOURTH AVE. NEW YORK 16, N.Y.

OPHTHALMIC INSTRUMENTS
OF PRECISION

Theodore Hamblin LTD

GUILD Rx OPTICIANS

15 WIGMORE STREET,
LONDON, W.1.
ENGLAND.

JUST EVERYTHING OPHTHALMIC
Rx SERVICE THROUGHOUT U. S. A.
DISPENSING—REFRACTING ADJUNCTS

●

*Beloccluders
Cataract Bifocal Loan Service
*Conacor Bifocal
Contact Lenses
Gonioscopic Contact Lenses
Guibor Amblyscope Charts
Guibor Distance Chart (E)
Guibor Hand Reading Card (E)
Guibor Motility Chart
Guibor Stereo Cards
*Hand Dual Occluder
*Belgard

*Hand Occluders
*Hand Prism Sets (glass-plastic)
*Hand Maddox Rods
*Hand Red Glass Comb.
Lebensohn Astigmometer
Lebensohn Hand Reading Card
*Lenscorometer
*Pocket Prism Bar
(Vertical ½-10Δ)
*Pocket Prism Bar
(Horizontal 3-20Δ)

*Phoro-Lenscorometer
*Portable Illum. Test Chart
Prism Bar 1-40
Prism Bar Vert. 1-25
*Prism Sets in Wallet
Red and Green Specs
Soft Rubber Occluder
Spec Bands
Stereoscopes
*Strait Top Bifocal Trial Set
Trifocal Trial Set
Worth 4-Dot Tests

DISPENSING SERVICE

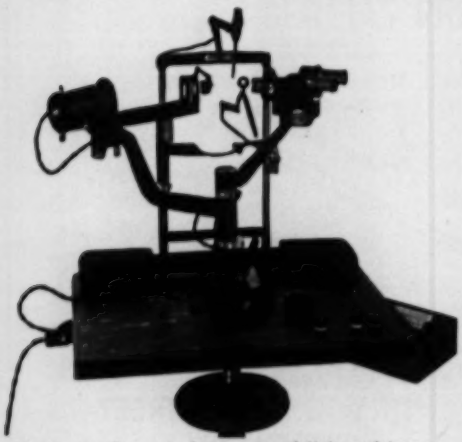
Main Office:
111 N. Wabash Ave., at Wash.
Chicago, Illinois

Austin Belgard INC.

OPHTHALMIC OPTICIANS
WHOLESALE & SERVICE

Branch Office:
1139 Central Ave., Wilmette, Ill.

"Take advantage of our Used Instruments Exchange when buying or selling used equipment of any kind. For information write to address below."



Trade in Allowance for Poser and Universal Lamps

The Unique
GOLDMANN SLIT LAMP

- One Arm Control
- Hruby Lens for Fundus Examination
- Many Other Advantages

U.S. Agents Also for:

Perimeters, Ophthalmometers and Other Ophthalmological Equipment.

Can Be Mounted on B & L or AO Stands.

ALFRED P. POLL
Ophthalmic Instruments of Top Quality
40 West 55th Street, New York 19, N.Y.

For the doctor who must do his own dispensing

Master Styling Room Ensemble

● Today's eye doctor must satisfy the growing demand of his patients for fashion, style and service. And at the same time, in the interest of more successful operation, he must increase his own efficiency.

After several years of research and study under actual operating conditions, PROFESSIONAL SUITE presents this matched line of equipment and furniture – *specifically designed and engineered for the modern styling and dispensing rooms of modern doctors* . . . sold in matched ensembles for large, medium and smaller offices. Individual pieces may also be purchased.

For further information on color, price, etc., discuss PROFESSIONAL SUITE with your supplier or send for this illustrated catalog.

Professional Suite

P. O. BOX 65
MINNEAPOLIS, MINN.

Professional Suite, P. O. Box 65, Minneapolis, Minn.

I'd like to take a look at your PROFESSIONAL SUITE catalog *(no obligation, of course).* Dept. No. AJ96

Name_____

Address_____

City_____ Zone____ State_____

GREINER & MUELLER

Expert makers
of artificial human eyes

GLASS & PLASTIC

55 E. Washington St. . . . Chicago 2, Ill.
Phone FR 2-4449
Branches at Kansas City, Mo., Detroit, Mich.

Our experts visit Milwaukee, Madison, Minneapolis, and St. Louis regularly. Serving the Middle West since 1924.

Eye making has been a family tradition with us since 1835.

Spectel
TELESCOPIC SPECTACLES

2.2x
(with Coated Lenses)

WHAT THEY ARE. A general discussion of the design, construction and uses of the improved Spectels. An outline of their development. Comparisons of the two magnifications and descriptions of the various trial sets. Bulletin 302.

HOW THEY ARE PRESCRIBED. Twelve pages of factual information on the application of telescopic spectacles. Case histories. Bulletin 304.

TRIAL PROCEDURE. A concise, step-by-step outline of the trial procedure which has been found effective. Bulletin 303.

TRIAL SETS. Complete descriptions and illustrations of the four different trial sets available. Form 85.

PRICES of Spectel telescopic spectacles, frames, trial sets and accessories are given in Form 7146-A.

This literature is available from your supply house or from

KOLLMORGEN Optical CORPORATION
NORTHAMPTON, MASSACHUSETTS

Distributed in Canada by Imperial Optical Company

TRANSACTIONS of the AMERICAN OPHTHALMOLOGICAL SOCIETY

Ninety-first Annual Meeting, White Sulphur Springs, West Virginia, 1955. Volume LIII

This latest volume in one of medicine's most important records of work-in-progress includes three theses of new associates in the American Ophthalmological Society, a report on "Fluorescent Materials for Orthoptic Training," and eighteen papers representing new findings and research in ophthalmology. Each paper gives in detail the experimental and clinical evidence on its subject and is followed by a full report of the discussion that took place at the meeting. *Illustrated.* $18.00

COLUMBIA UNIVERSITY PRESS, New York 27

For the Discriminating Eye Physician
Depend on the Services of a Guild Optician

GUILD OPTICIANS Rx

IN LYNCHBURG, VA.
A. G. JEFFERSON
Ground Floor Allied Arts Bldg.
Exclusively Optical

IMPORTED TRIAL SET

A handsome office trial set to be proud of! Fitted, velvet lined polished hardwood case, finished in blonde. Highest quality 1½" standard trial lenses in a wide, logical assortment, including 140 spheres, 44 cylinders, 12 prisms, 16 accessories, 2 trial frames, P.D. measure and rule. . .$125.00 f.o.b.

Unconditionally Guaranteed

Optical Import Co.
BELLINGHAM, WASH.

It Will Pay You

•

to look through the advertising pages of this Journal.

We discriminate as to the quality and reliability of the advertising accepted for the

•

AMERICAN JOURNAL *of* OPHTHALMOLOGY

NEW YORK EYE AND EAR INFIRMARY

POST GRADUATE SCHOOL

●

Course in

Histopathology of the Eye

Oct. 1-6, 1956—2 to 6 P.M. each day

Fee $100

●

Address **Registrar**
218 Second Ave. N.Y.C. 3, N.Y.

ANNALES D'OCULISTIQUE

One of the oldest ophthalmological reviews. Founded in 1838 by Florent Cunier, continued by Warlomont (1853), Valude and Sulzer (1891), V. Morax (1898).

The Board of Editors is as follows:

REDSLOB	ROCHON-DUVIGNEAUD	MAGITOT
BAILLIART	JEANDELIZE	HARTMANN
HAMBRESIN	LEPLAT	FRANCESCHETTI
AMSLER	P.-V. MORAX	PAUFIQUE
DIAZ-CANEJA	FRANÇOIS	MAGGIORE

Editor-in-Chief: Dr. A. MAGITOT 9 R. de MARIGNAN (Paris)

The publication includes original articles, notes on practical ophthalmology, descriptions of clinical cases and reports of the proceedings of European ophthalmological Societies.

This review is published by Messrs. Doin & Co.
8 Place de l'Odeon Paris 6e

Subscription rates: France and Colonies—4000 Frc.
Abroad —4200 Frc.

KEELER HEADBAND TRIAL FRAME

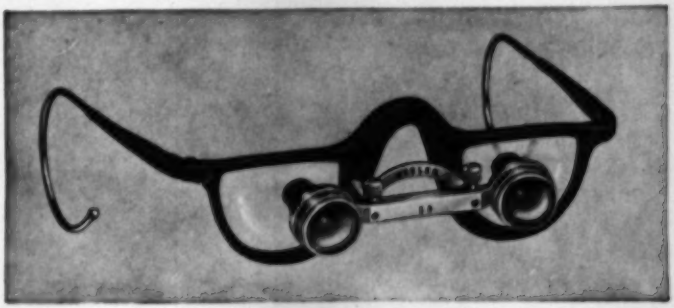
A simple, time-saving and versatile frame ideal for the busy practitioner.

- Double universal joints eliminate bridge and sides—speed and simplify centering on asymmetrical faces.
- Back Vertex Distance easy to adjust and simple to measure accurately—invaluable for aphakics and high myopes.
- Absence of bridge facilitates accurate location on children.
- Firm yet comfortable headband is less distracting for children than conventional devices.

OUTSTANDING EQUIPMENT

KEELER MAGNIFYING SPECTACLE

Each individually made to user's own prescription



- Remarkably flat, color-free 35mm field.
- Magnification X 2.2.
- Gaze can alter from central, magnified, field to peripheral, unmagnified, field without change of focus or position.
- Unique "slip-on" telescope assembly for rapid, simple cleaning.

KEELER OPTICAL PRODUCTS INC.

617 S. 52nd Street, Philadelphia 43, Pa., USA

GRANITE 4-5310 & KINGSWOOD 4-0874

"58"

SCORES AGAIN IN THE

Tillyer "D"

BIFOCAL WITH A

22mm Segment

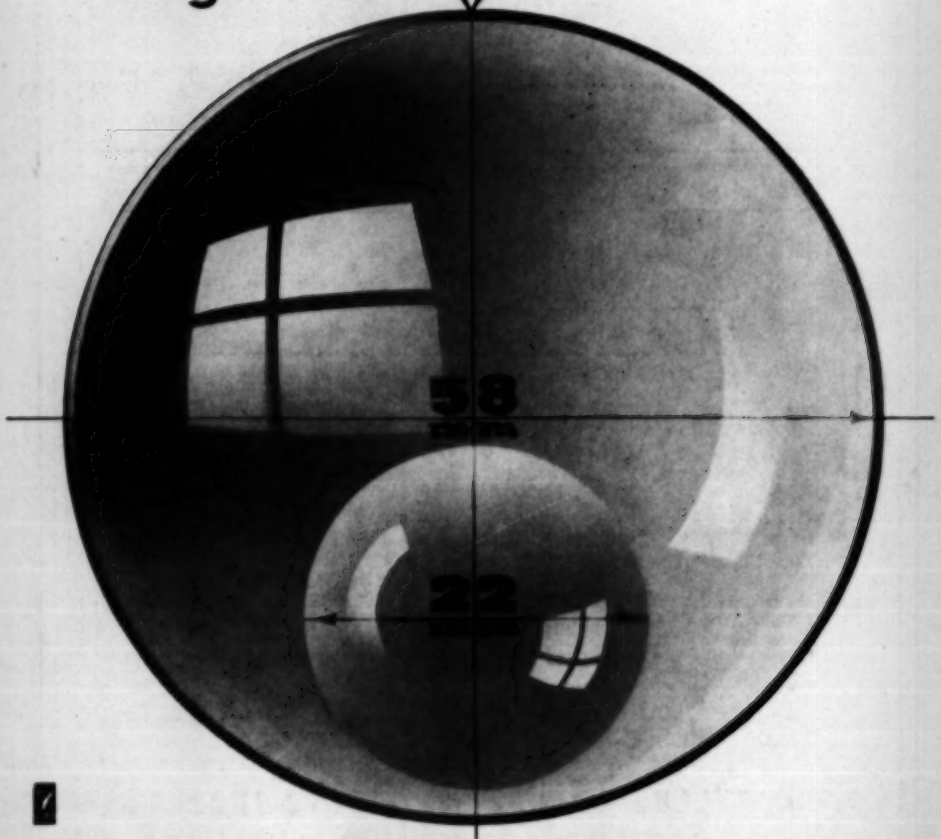
Outstanding Characteristics of the New Tillyer D Bifocal

- New 58mm blank
- New 22mm round segment
- Fused barium segment
- Nearest thing to bifocal invisibility
- Maximum marginal correction based on famous Tillyer principle

AVAILABLE IN:

White • Cruxite A • Cruxite AX • Cosmetan* Calobar D*

*with colored segments



American Optical